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*Meyer, E., and Arnold, L., *Amer. J. Digest. Dis.*, 5:418.

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The Australian and New Zealand
JOURNAL OF SURGERY

Vol. 26 — No. 4 MAY, 1957

CASE OF LINGUAL THYROID WITH SUCCESSFUL GRAFTING AFTER OPERATIVE REMOVAL

By Robert S. Lawson

Melbourne

LINGUAL thyroid is a rare condition and when present it may be symptomless. However, in reported cases, symptoms of voice changes, dysphagia, or respiratory obstruction of varying degrees are usually mentioned. Less often, haemorrhage has occurred from the exposed surface of the gland, and in very rare cases, there have been malignant changes, or thyrotoxicosis has developed.

FIG. I. Appearance of the lingual thyroid before operation.

FIG. II. Appearance of the lingual thyroid at operation. The tongue is being pulled out by transfixing sutures of catgut, and the lingual thyroid is being lifted forwards by a finger behind it.

When any of these symptoms have made it necessary, removal of the lingual thyroid has been performed, either by the per-oral approach or after lateral pharyngotomy, each of these methods having its advocates.

In 70 per cent. of reported cases of lingual thyroid, there has been no thyroid tissue in the normal situation. In these, removal of the gland has necessarily produced a state of hypothyroidism, requiring a maintenance dose of thyroid to be given regularly and permanently thereafter. In order to avoid this, deliberate partial removal has been tried, but this has proved unsatisfactory. Further development of the remaining thyroid gland tissue may occur with return of symptoms (Ackland, 1955). Treatment by radioactive iodine is also unlikely to be successful in reducing the bulk of tissue sufficiently to relieve symptoms. It would appear that complete removal of the gland is required to ensure permanent relief. Attempts have therefore been made to avoid the need for post-operative thyroid medication by grafting the thyroid gland after removal. Swan, Harper and Christensen (1952) had some success in implanting the excised lingual thy-

roid into the rectus abdominis and pectoral muscles, and the account which they give of their experiences, both clinical and experimental, is of value to anyone interested in this problem.

The following case is reported because it appears that grafting of the lingual thyroid gland after its removal has been completely successful, at least after an interval of about a year.

FIG. III. The patient before operation.

CASE REPORT

B.M., a slim child of 11 years, was brought in by her mother to see Dr. Dudley Hagger in August, 1955, with the complaints that her voice was peculiar (speaking as if she had a plum in mouth), and her breathing sometimes appeared difficult. These symptoms had been greatly aggravated during a recent attack of acute pharyngitis, causing a good deal of apprehension. She had always slept with her mouth open. Her tonsils and adenoids had been removed in early childhood ("for snoring"), but with no benefit.

Dr. Hagger recognized the condition responsible for her symptoms as a lingual thyroid. This formed a sessile projecting swelling, like a flattened strawberry, over the posterior third of the tongue. It was firm and evidently solid but paler in colour than the normal tongue surface and of a different consistency. It could be seen readily enough when the tongue was fully protruded (Fig. I). Tests with radioactive iodine confirmed the diagnosis and also indicated that there was no thyroid gland in the normal situation.

The patient was presented at a meeting of the Pediatric Society of Victoria in October, 1955, a number of experienced pediatricians and surgeons being present. The rarity of the condition was attested by the fact that no one present had previously seen a case of lingual thyroid. It was mentioned that five cases had received treatment at the Lahey Clinic, Boston, out of a total of some 25,0[illegible] patients treated surgically for goitre (Cattell, 1955). After full discussion at this meeting, it was agreed that surgical treatment should be undertaken, as it was felt that symptoms were likely to be progressive, with aggravation at the onset of puberty. The child at this time appeared to be flat-chested and underdeveloped, but otherwise healthy (Fig. III).

Accordingly, plans were made for the operation. It was decided to attempt removal by the per-oral route, but preparation was made to perform pharyngotomy if necessary, and also tracheotomy should it be required.

Operation was performed on 11th January, 1956, under general anaesthetic administered by Dr. Gordon Houseman, who intubated the larynx blindly through the nose. After gagging the mouth wide open, the tongue was pulled forward with three transfixing sutures of stout catgut on each side, thus bringing the lingual thyroid into view. Passing a finger behind the thyroid swelling, it was discovered that it hung down over the epiglottis, and was larger in bulk than had been anticipated. It was possible with a finger behind it to "dislocate" it forwards, bringing it up to the level of the teeth (Fig. II).

The removal proved to be not a matter of great difficulty. Dissection in front opened up a plane of cleavage and the gland was then shelled out of its bed in the tongue rather after the manner of enucleation of the prostate. The main vessels appeared to enter the gland postero-laterally on either side, close under the mucous covering at these sites. These vessels were secured, and removal was completed by further sharp dissection. The considerable trough or hollow in the surface of the tongue was then closed by deep transfixing sutures of catgut passed from behind forwards, thus largely obliterating the gap.

The patient's condition appearing to be satisfactory, it was decided to attempt grafting of the excised thyroid tissue. The exposed surfaces of this mass were sliced off to remove those parts contaminated with saliva including the exposed mucous epithelial lining. This left a cube of tissue with sides rather less than 1 in. long. This cube of thyroid gland was then sliced with a knife, like cutting a loaf of bread, into about a dozen very thin slices. These were then implanted in small pieces

into the lower half of the right rectus abdominis muscle. Successive gaps were opened in this muscle, the small pieces were dropped in and the muscle was sutured over each gap with fine plain catgut, the rectus sheath being closed over all. A blood transfusion was then given and the patient returned to bed.

FIG. IV. The patient 10 months after operation.

There was some anxiety that night because of respiratory obstruction. However, tracheotomy was avoided and thereafter the patient made a smooth recovery. Both the tongue and the abdominal wound healed cleanly and the patient went home 10 days after operation.

The child returned to school after the summer holidays and has been very well since. Further tests with radioactive iodine performed eight months after operation indicated "no uptake in the sublingual region but an estimated uptake of 18 per cent. of the dose in the region of the graft which therefore would appear to be functioning." At this time the basal metabolic rate estimation gave a figure of −1 per cent. compared with a reading of −5 per cent. prior to the operation.

The patient was again presented at a meeting of the Pediatric Society in September, 1956, and she appeared to be very well. She was speaking normally and the tongue was smoothly healed. Her mother stated that she was sleeping with her mouth shut which she had not done before, and her general state of health had improved. No thyroid treatment had been given at any stage. Her weight had increased from 74 lbs. (December, 1955) to 88 lbs. (August, 1956), height from 5ft. 1 in. to 5 ft. 2½ ins. There was no suggestion of hypothyroidism in her clinical appearance. The flatness of the chest had disappeared, and though not yet menstruating, she gave the appearance of being in early puberty.

It is still too early to make any final assertions about the success of the grafting procedure, and the child's future development will be followed closely. However it can be stated that after nine months her health is completely normal. She looks a vigorous young citizen as can be seen from the photograph (Fig. IV).

ACKNOWLEDGEMENTS

It is a great pleasure to acknowledge with gratitude the confidence of Dr. Dudley Hagger who entrusted the surgical treatment of this patient to my care. The per-oral approach to the operation and the decision to attempt grafting were largely due to his influence in urging them, as being in the patient's best interests.

We are much indebted to Dr. Keith Fairley for his advice and for information on the radioactive iodine tests, and also to Dr. Richard Cattell of the Lahey Clinic for helpful advice on the operative procedure.

Mr. N. Talbot Hamilton assisted at the operation. The photographs for Figs. I, III and IV were taken by Mr. Scrimgeour while the photograph of the appearances at operation (Fig. II) was kindly taken by Mr. E. S. R. Hughes, who interrupted his work in an adjacent operating theatre in order to take this picture impromptu.

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POST-MORTEM HOMOGRAFTS IN EXTENSIVE BURNS

By Neville C. Davis

Brisbane

IT is a wonderful thing that an individual even after death may save the life of another. This is now possible with the use of post-mortem homografts in the treatment of extensive burns. The method has been developed by Barrett Brown (1953, 1954, 1955) in the United States but, as far as can be ascertained, has been little used in Australia. Perhaps this is because Burns Units are not common in Australia and because the case requiring homografts for survival is not common in civilian practice.

A case is reported where it is believed that the use of post-mortem homografts was life-saving.

Case Report

R.P., a fit young man of 23 years of age, was admitted to the Brisbane General Hospital on 10th January, 1956, suffering from severe burns. He was a motor mechanic and had been burning off some rubbish behind the garage two hours prior to admission when a drum of petrol exploded and burnt him.

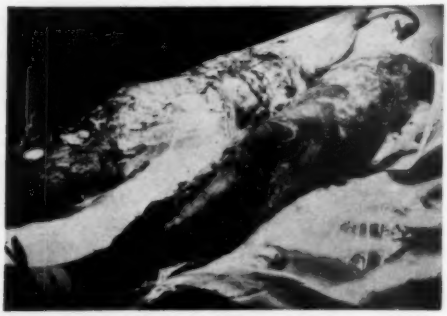

FIG. I. Full thickness burns of the lower limbs treated by the exposure method. Photograph taken on the 23rd January, 1956, thirteen days after admission.

There were circumferential burns of both lower limbs and both upper limbs and burns of the buttocks and most of the back of the trunk. It was estimated that the total burn involed 55 per cent. of the body surface area, of which about 35 per cent. was full thickness. Resuscitation was instituted by Dr. J. C. A. Dique, using albumin and electrolyte solutions. The upper limbs were cleaned with Zephiran, then occlusive dressings applied with the hands elevated in the position of function. The lower limbs were treated by the exposure method. To implement this, Steinmann's pins were inserted into each heel and a sling placed behind each knee. The patient lay on his back with *tulle gras* and combined dressing intervening between the burn of the trunk and the sterile sheets. An in-dwelling catheter was inserted to enable a constant check to be kept on the urinary output. Penicillin in high dosage and morphine were prescribed.

Next day his general condition was very satisfactory. Intravenous therapy was continued and included two litres of blood as well as albumin and electrolyte solutions. By the 14th January he was taking oral fluids satisfactorily, and the catheter was removed. On the 18th January, some of the full thickness burns were beginning to separate, in part with the aid of maggots. By the 22nd January, he was becoming toxic, was confused and distended. From the burns were cultured B. pyocyaneous, B. coli, and B. proteus resistant to all the usual antibiotics (Fig. I).

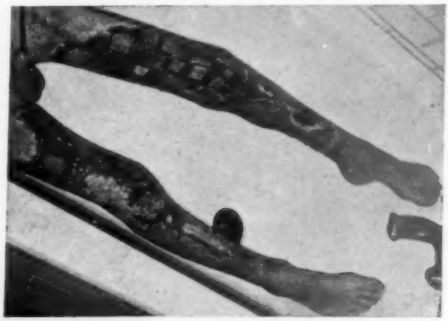

FIG. II. Photograph of patient taken on the 13th February, 1956. Note homografts, autografts and pinch grafts. Both tibiae are exposed.

On the 23rd January, under general anaesthesia, approximately half of the infected full thickness burns were excised from both lower limbs. It was considered wise to do this excision in stages because of the risk of shock. Occlusive pressure dressings were applied and the limbs elevated. The antibiotic was changed to tetracycline.

By this time it had become obvious that it was a matter of urgency to cover the raw areas with skin. Unfortunately, the patient's general condition precluded the use of autografts even if enough suitable areas had been available. Therefore, it was decided to use homografts to tide the patient over this critical period.

On the 24th January, under full aseptic technique in the general operating theatre, split skin grafts were cut from a deceased lady of 67 years of age. She had died suddenly eleven hours previously of a cerebal haemorrhage and the cadaver had been refrigerated. The grafts were cut with Humby and

Blair knives, were wrapped in penicillin-saline gauze and kept in the refrigerator used for storing blood.

On the 27th January, the major part of the remaining burns slough was removed from both lower limbs and from the right arm under anaesthesia. The sloughs extended right down to the tibia on both sides and the anterior tibial compartment was infected and necrotic. Trypure was injected under the small remaining areas of slough.

On the 31st January, in the ward without any anaesthesia, the post-mortem homografts were applied as postage stamp grafts to the left lower limb.

FIG. III. Photograph of patient taken on the 13th February, 1956. Note the difficulty of distinguishing homografts from autografts.

On the 3rd February, under general anaesthesia, the remaining sloughs from the front of the thighs were excised. Pinch grafts, homografts and autografts were applied to both lower limbs with particular attention to the posterior aspects. The split skin autografts were cut from both arms and the back which had now healed. These various types of grafts were scattered haphazardly over the raw areas of the lower limbs. It was noted that there had been an almost complete take of the homografts to the left lower limb. The antibiotic was now changed to chloramphenical.

On the 7th February, he was given a saline bath and it appeared that most of the autografts had taken. Further homografts were applied — the donors on this occasion being patients undergoing grafting for various reasons four days previously. The grafts once again had been wrapped in penicillin-saline gauze and kept in the refrigerator until required for use.

On the 10th February, with the patient in the bath, it was difficult to tell which were homografts and which autografts. His general condition was very satisfactory but both tibiae were exposed for about six inches and the left tibia was beginning to sequestrate (Figs. II, III, IV).

On the 16th February, the pinch grafts were showing signs of spreading but there was no sign of disintegration of the homografts.

On the 20th February, under general anaesthesia, sequestra were excised from each tibia with a chisel and the healthy raw surface covered with fresh autografts. Exuberant and unhealthy granulations were excised and some of the resulting raw area was covered with autografts. Coverage was limited by the shortage of donor sites.

FIG. IV. Photograph of patient taken on the 18th February, 1956. Note the good morale of the patient and the healing of the burns of the upper limbs and hands.

On the 25th February, the burns dressings were removed and the patient placed in a saline bath. For the first time, it was noted that the original post-mortem homografts were now being absorbed leaving an infected granulating surface. The recent autografts did not appear to have taken well.

On the 5th March, further split skin autografts and pinch grafts were applied under anaesthesia. Extreme difficulty was noted in finding donor sites. The grafts were cut free hand and with the Paget's dermatome from the chest and the right arm. Pinch grafts were taken from sites unsuitable for dermatome and free hand grafts.

By the 15th March, the major part of the burn was healed. He was allowed up and physiotherapists encouraged him to walk with calipers. He maintained steady improvement and was discharged from hospital on the 16th April, 1956 (Fig. V).

He was re-admitted on the 1st May, 1956, with infection of the grafted areas of his legs. His wife had recently been confined and he had spent a lot of time going to and from the hospital. The infection responded rapidly to antibiotics and he was discharged again a week later.

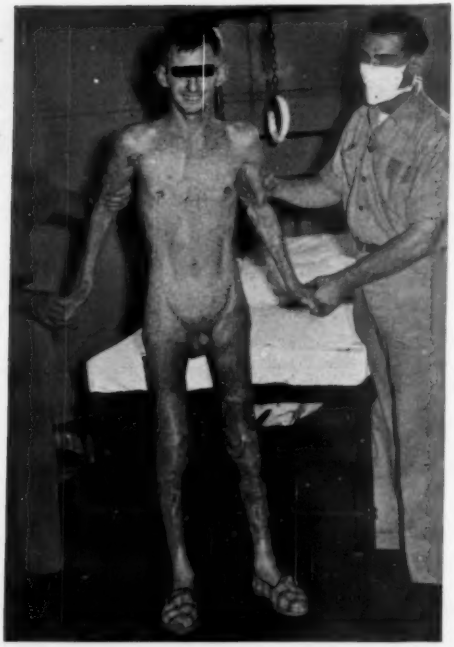

FIG. V. Photograph of patient on the 7th April, 1956. Burns now healed.

He has been seen regularly since as an outpatient, and, on the 17th July, 1956, stated he could walk a mile without difficulty (Fig. VI).

DISCUSSION

Great progress has been made since the Second World War in the management of burns. By dint of careful but vigorous resuscitation, patients with severe and extensive burns are prevented from dying of shock in the first days following the burn. However, many of these patients live to die at a later date from infection or toxaemia due to the open wound. These patients would be saved by covering the raw areas with skin grafts at the earliest possible moment. In many cases of extensive burns, however, it is not possible to obtain the necessary area of autografts because of the poor general condition of the patient and the lack of availability of the donor areas. In such cases, resort to postmortem homografts will often tide the patient over this critical period until he can supply his own skin either by growing in of epithelium from the periphery or by the healing of suitable donor sites. Homografts will improve the general condition, reduce the fever and enable the patient to take a full diet.

FIG. VI. Photograph of patient on the 17th July, 1956 — seven months after burn. He could then walk a mile without difficulty.

Certain points are of interest in this particular case. The fact that he was a healthy young man with a fighting spirit made a tremendous difference. Older patients and those with poor morale would not have survived. One should not embrace a particular form of treatment but adapt it to the patient. Thus, exposure treatment was ordered for the lower limbs and occlusive dressings for the upper limbs. It is difficult to expose circumferential burns so Steinmann's pins were inserted into the heel to elevate the limb

and thus reduce pressure on the posterior aspect. Pressure plus exposure must surely be the worst form of burns treatment. Throughout the course of the illness, regular estimations of the haemoglobin percentage and bacteriological examinations were made. Appropriate intravenous and antibiotic therapy was ordered.

The treament of major burns may be summarized as being the surgical replacement of full thickness burns by skin grafting at the earliest possible moment. Certainly the author believes that grafting must begin no later than the twenty-first day, otherwise the surgeon must search for a valid reason for delay. Full thickness burns will not separate under twenty-one days unless they are surgically excised. The use of enzyme debriding agents such as Trypure leaves much to be desired — except in minor burns which are not dangerous to life. However, the excision of the burns slough is a serious operation and should be done in stages to prevent severe shock. Elevation of the limbs during and after the operation will reduce the blood loss. If skin grafts are applied at the same operation as the sloughs are excised, there is a danger that inadequate haemostasis will cause the grafts to fail to take.

When homografts are used, it is a good idea to scatter small autografts and pinch grafts between them. By this means, the autografts will be spreading by the time the homografts disintegrate. It is quite difficult sometimes to tell which are autografts and which homografts. The homografts appear viable until about the third or fourth week when they suddenly disintegrate.

SOME POINTS CONCERNING HOMOGRAFTS

A series of live donors is no longer required for one badly burned patient—large amounts of skin may be taken from a single donor after death and used immediately or set aside in a refrigerator for later use. There is no disfigurement, time loss or wound care necessary for such a donor.

Permission must be obtained from the relatives of suitable deceased patients before cutting the homografts. There is rarely any difficulty when the position is put before them. Certain cases are unsuitable as donors — for example, those with infective lesions, those with malignant disease and those who have died more than six hours previously without the benefit of refrigeration.

The excision of the homografts should be done with full aseptic precautions in the operating theatre. This can be arranged discreetly with the co-operation of the theatre staff. Thin grafts should be cut as they are just as effective as thick grafts and their temporary take is better.

The relatives of the burned patient should be told that as a life-saving measure the skin from another person is to be used. The patient himself may state, as this lad did during his recovery, that he prefers "the skin from the bank rather than his own — as it doesn't hurt so much!"

The homografts may be used immediately or may be kept wrapped in penicillin-saline gauze at the temperature of the ordinary household refrigerator. Just how long they will keep is not known but the author has used with success autografts which have been refrigerated for fourteen days.

Permanent persistence of homografts has never been established in humans except in identical twins. There is no relation between the blood groups of donor and recipient and the amount or permanence of the take. After some initial enthusiastic reports ACTH has proved ineffective for prolonging the life of homografts. It should be emphasized that autografts should be applied to replace homografts as soon as the patient is fit and has enough of his own skin available.

SUMMARY AND CONCLUSIONS

1. A case is reported in which the use of post-mortem homografts for the treatment of severe and extensive burns was considered to be life-saving.
2. In many cases of extensive burns it is not possible to use autografts because of the poor general condition of the patient and the lack of availability of donor sites.
3. With atomic warfare looming in the future some thought should be given to the use of homografts on a large scale. Most members of the public, if they knew, would be prepared to offer their skin after death to save the life of another person.

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THE SURGERY OF MAJOR ARTERIAL OBSTRUCTION AND OCCLUSION

By Rowan Nicks

From the Thoracic and Cardiovascular Unit, Green Lane Hospital, Auckland; now of Royal Prince Alfred Hospital, Sydney

THE simple trust of wounded comrades has inspired a generation of war surgeons and their associates to investigate further, in the light of peace-time reflection and experiment, many problems dealt with summarily on the battlefield, and constantly recurring amid the shocks and accidents of modern life.

Much has been learned in the wide field of traumatic surgery including techniques for restoring injured, obstructed and aneurysmal blood vessels. This paper deals briefly with some congenital and acquired types of arterial obstruction and occlusion within our experience.

The congenital obstruction is commonly a thoracic aortic coarctation and differs from other types in that life is threatened more by the strain on the heart and vascular system than by ischaemia of the limbs.

The acquired occlusions to be considered are due to accidental trauma, surgical interruption, embolism and arterial degeneration.

(a) Trauma results in acute arterial spasm or thrombosis on a raw or roughened surface after partial or complete rupture and retraction of the intimal and medial coats, often without damage to the tunica adventitia (Learmonth, 1940) (Fig. I).

The obstruction is at first local but may extend centrally and peripherally by secondary thrombosis if there is stasis, and if the injury to the vessel is severe. The prognosis is determined by the site, the length of vessel involved and the disposition of major collaterals. The associated arterial spasm is of local smooth muscle origin, not under nervous control, and is sensitive to smooth muscle relaxants such as papaverine 4 per cent. locally applied (Kinmonth, 1952). Limbs surviving without surgical restoration are frequently left with symptoms of chronic vascular insufficiency and occasionally with an arterial aneurysm if the proximal end remains in direct communication with a weakness or rent in the vessel wall (Case 1, Fig. IIa and IIb). Local thrombosis may also

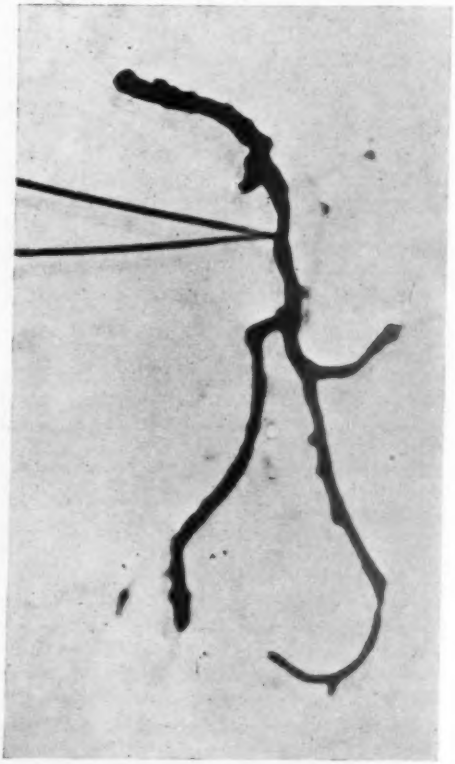


FIG. I. Thromboscd popliteal and tibial arteries. The patient, a Jugoslav naval officer, was blown up by a sea mine, sustaining bilateral dislocation of the knees, for which amputation of both legs was performed. The dissected vessels were thrombosed up to the line of section and there was a complete fracture and retraction of the medial and intimal coats (opposite the pointer) with preservation of the adventitia.

be induced by minor trauma, especially if the vessels are inelastic and atherosclerotic with narrowing and irregularity of the lumen along the whole peripheral bed which, by itself, greatly impedes the blood flow (Case 2, Fig. IIIa and IIIb). Thrombosis of an arterio-

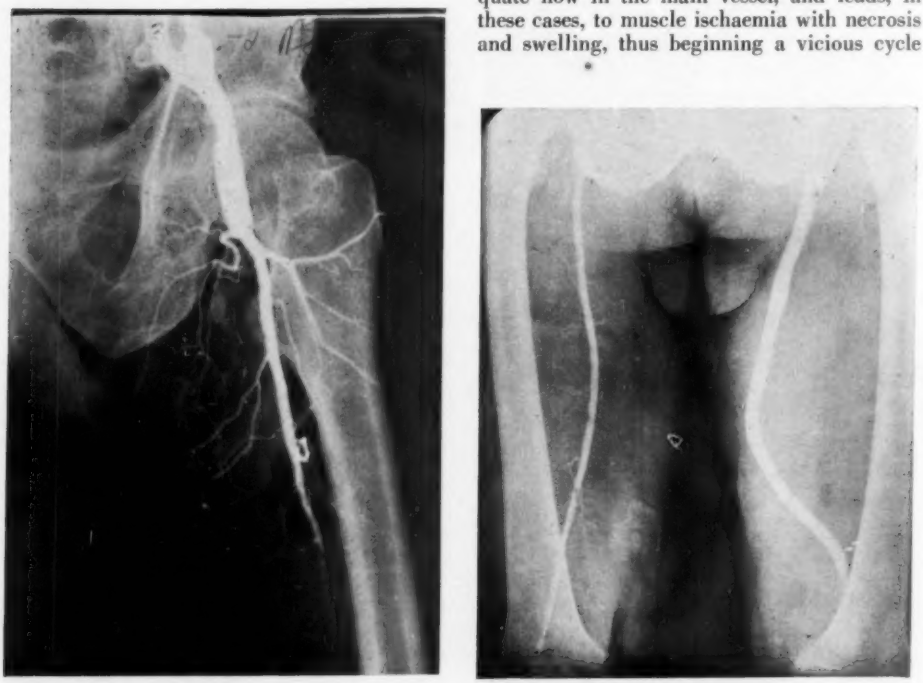
(a) (b)

FIG. II. (Case 1) F.E., 45 years. Popliteal aneurysm sequel to disruptive injury to the knee joint.
(a) False aneurysm of the popliteal artery.
(b) Two years after excision and replacement by an autogenous vein graft.

sclerotic femoral artery frequently originates at the fixed point of the adductor opening in the thigh (to which the vessel is fixed by a reflection of adventitia) on the basis of minor intimal haemorrhage after bending (Mavor, 1955). Trauma of muscular origin occurring at the site of a similar attachment of the popliteal artery to the capsule of the knee-joint is considered the basis of primary popliteal thrombosis in young people (Learmonth, Blackwood and Richards, 1944; Boyd, 1949).

(b) *Surgical interruption* is sometimes accidential, viz. ligation of the femoral artery instead of the saphenous vein (Case 10); but more frequently is deliberately performed to make possible excision of a tumour (e.g.

carotid body) or of an arterio-venous fistula. Interruption of the main vessels of the leg is usually followed by symptoms of vascular insufficiency including coldness, intermittent claudication and fatigue (Case 3.).



(a) (b)

FIG. III. (Case 2) J.M., 67 years. Superficial femoral thrombus following trauma, Arteriograms showing:

(a) Superficial femoral thrombosis with vascular insufficiency to the foot despite sympathectomy and good collaterals.

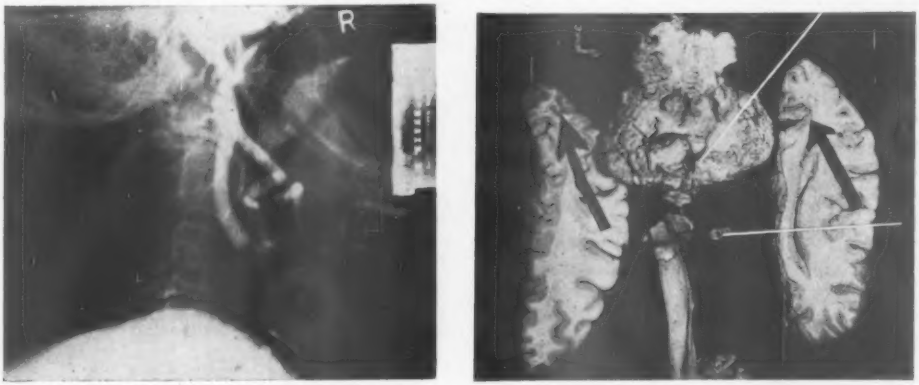
(b) Following insertion of a common femoro-popliteal by-pass graft. The collaterals are not in evidence. The right femoral artery has developed a segmental thrombosis.

In the arm, division of the first part of the subclavian artery and its main branches at the root of the neck has been performed routinely prior to anastomosing the central end with the pulmonary artery in the Blalock operation for Fallot's tetralogy, without giving rise to disability.

(c) Systemic embolism most frequently occurs in cardiac cases, the clot usually being arrested at, and completely occluding, the important collateral circulation rising in the vicinity of a major arterial bifurcation, as well as the axial flow. The occlusion, which may be partial at first, is completed by accretion and propagation of blood clot which usually extends peripherally if the collateral circulation is insufficient to maintain an adequate flow in the main vessel, and leads, in these cases, to muscle ischaemia with necrosis and swelling, thus beginning a vicious cycle of progressive ischaemia from compression of collaterals within aponeurotic compartments, which, if not arrested within twelve hours, is irretrievable. The associated arterial spasm is strictly localized to the occluded segment, the vessel beyond being collapsed owing to diminished blood flow. The embolus is plugged firmly into the tapering artery, locally distending the wall, which is at first congested and oedematous but intact, and only later becomes necrotic and fixed by inflammation.

Clinically, the site of the embolus is indicated by the distribution of pain, being referred to the abdomen, buttock and upper thigh in aortic embolism and to the lower third of the thigh and the calf in femoral and popliteal embolism respectively. It is dependent on muscle ischaemia and disappears only after the restoration of a satisfactory circulation. Ischaemia of the peripheral nerves is responsible for tingling, loss of sensation and paralysis of muscles. Rheumatic valvular disease has been responsible for only 4 of 21 peripheral emboli occurring at the Green Lane Hospital over the past ten years, and this number will probably be lessened in future by earlier recourse to valvotomy for mitral stenosis, especially in cases with a history of previous embolic episodes.

lining and the duration of obstruction. It has been suggested (Barker, 1948) that interference with the heparin cycle may predispose to intravascular clotting. It is a localized complication of general atherosclerosis involving to a greater or lesser degree the arteries to the heart and brain (the latter being open to inspection via the retinal arteries) as well as those already mentioned (Case 4, Fig. IVa and IVb). A good collateral circulation developed slowly over a long time, may be enough to minimize symptoms and conceal the insidious progress of the disease — whereas thrombosis of sudden onset, often involving long lengths of the vessel and its collaterials, gives rise to immediate concern, and may lead to gangrene.



(a) (b)

FIG. IV. (Case 4) N.M., 61 years. Diagnosis: Thrombosis of the right internal carotid artery. Resection under hypothermia.

(a) Arteriogram showing narrowing of the origin of the internal carotid artery.

(b) Post-mortem specimen of the brain showing recent thrombus in the basilar artery and infarction of the calcarine fissure. The resected segment of the carotid artery and the reconstruction is figured below.

(d) Degenerative arterial thrombosis, which is often segmental to begin with, may occur either spontaneously or following minor trauma in atherosclerotic vessels and may, or may not, be accompanied by an increase in the blood cholesterol. It occurs frequently in the terminal aorta, common iliac, femoral and popliteal vessels, and is of varying length depending on the volume of collateral blood flowing into the main vessel, the state of the

TREATMENT

The surgical ideal, which is to relieve a localized obstruction and restore the axial flow, is often unattainable, especially in cases associated with degenerative arterial disease; and for cases in this category, improvement of the nutrition distal to the obstruction, relief of intolerable pain, and amputation for gangrene may be accepted as lesser goals.

(1) *Congenital coarctation of the aorta*

In the common variety, the surgical problem is the technical one of resection of the stricture and re-anastomosis, usually without recourse to an aortic graft, for during the period of occlusion the vital organs are safe from ischaemic hazard because of the well-developed collateral circulation.

Thirty-one cases have been explored in this Unit and anastomosis effected in 30, with two deaths in the series, one from haemorrhage and one probably from anoxic brain damage following the sudden lowering of the cerebral arterial blood pressure below that to which the vital centres were accustomed to receiving oxygen. In one case complicated by haemorrhage, in which it was necessary to suture both ends of the aorta, the convalescence was uninterrupted and the patient's clinical condition has not deteriorated subsequently in two years. It is anticipated that grafting will have to be undertaken some time.

In the remaining 28 cases there were no serious complications and a follow-up in 21 of these over a minimum period of six months showed the blood pressure and general activity to be restored to normal in 18 and to be greatly improved in 3.

(2) *Traumatic arterial obstruction*

The great single advance in the treatment of open wounds involving a major artery has been an increase in knowledge of the problems concerned with primary wound healing, namely, wide excision of damaged tissue, the release of confining aponeurotic compartments so as to allow muscular swelling without compression of the blood vessels, and the control of bacterial infection.

On the basis of surgical experiment in dogs, Miller and Welch (1949) confirmed wartime stress on the time-lag between arterial interruption and treatment, showing that there was complete recovery if the repair were done within six hours, but only partial, and with permanent ischaemic contracture in the 24 per cent. which survived twenty-four hours of occlusion.

The dramatic fall of the amputation rate for limb injuries from 49 per cent. in the Second World War to 10.3 per cent. in the American Forces in the Korean War for wounds inflicted by similar missiles, gives inspiring confirmation of the soundness of these principles. Ligation of the femoral and subclavian arteries under battle conditions in the First World War was followed by amputation in 25 per cent. of cases and of the popliteal in 41 per cent. As a consequence of higher velocity missiles fired in the Second World War there was a general increase in the amputation rate to the 49 per cent. previously mentioned which, for the popliteal artery, had risen to 72 per cent. (de Bakey and Simeone, 1946).

The successful introduction of arterial suture and grafting for the immediate treatment of arterial injuries behind the front line in Korea realized the vision of previous war surgeons and was the pilot of peacetime developments. Of 56 cases in which arterial repair was performed (48 end-to-end and 8 vein grafts) only 6 failed (Jahnke and Seeley, 1953). Of 28 cases with limbs surviving major arterial injury treated by ligation, 30 per cent. showed arterial insufficiency despite lumbar sympathectomy.

The residual disability from vascular injury of the lower limb and the possibility of early and late reconstruction in selected cases is summarized in the table constructed from information made available from the Pensions Department for vascular injuries in the whole New Zealand Armed Forces in the Second World War, 1939-1945 (Table 1).

The problem of war wounds is more complicated than peacetime injuries for many reasons, the chief being the high velocity of the missiles, causing wide necrosis of tissue and infection, the frequent multiplicity of wounds (often accompanied by profound shock), the particular strategic circumstances and location of the battle, with consequently a widely varying time-lag between wounding and the institution of adequate surgery. The feasibility of performing meticulous and time-consuming operations must be considered against this background.

The main problems of treatment presented by a case of acute arterial injury in peace as in war are diagnosis and subsequent restoration of the circulation to the ischaemic limb as soon as possible. Apart from direct injury, discussed above, arterial injuries are

TABLE 1

NEW ZEALAND ARMED FORCES — SECOND WORLD WAR — ARTERIAL WOUNDS INVOLVING MAJOR ARTERIES

ANALYSIS OF 57 SURVIVORS WITHOUT AMPUTATION

(By the courtesy of the Medical Director-General)

Vessel	*Number*	*Symptoms*	*Pension*
UPPER EXTREMITY:			
Subclavian artery	1	Nil	Nil
Axillary artery	8	Vascular insufficiency (contracture) 3	Mainly for nerve and joint injury:
			25-30 per cent. 4
			50 per cent 2
			75-80 per cent. .... 2 (1 contracture)
Axillary vein	2	Vascular nil	10-25 per cent.
Brachial artery	10	Vascular nil	Disability non-vascular:
			Nil-15 per cent. 4
			25-45 per cent. 5
			60 per cent. 1
HEAD AND NECK:			
Common carotid	2	Dizziness and head noises 2	25-30 per cent. 2
		Upper motor neurone 1	
LOWER EXTREMITY:			
External iliac artery	1	Muscle cramps	50 per cent.
Internal iliac artery	1	Nil vascular	40 per cent.
External iliac vein	1	Cramps, swelling, ulcer	30 per cent.
Femoral artery	11		
	Interruption 9	Nil 2	Nil 2
	Aneurysm 1	Muscle cramps 9	10-25 per cent. 6
	A-V fistula 1	Contracture 2	60-70 per cent. 3
Femoral vein	2	Cramps	30-40 per cent. 2
		Swelling	
Popliteal artery	6	Cramps 3	Nil 1
	A-V fistula 4	Nil 1	15-30 per cent. 3
	Interruption 2	Cramps and S.T. 2	30-60 per cent. 2
Tibial arteries	12	Mainly non-vascular	Nil 3
			10-25 per cent. 4
			30-40 per cent. 3
			60-70 per cent. 2

encountered most frequently in fracture dislocations about the knee and elbow joints (Griffiths, 1944) (Case 5).

The diagnosis of arterial injury, indicated by extreme pallor and tingling in the limbs and rapidly developing muscular paralysis with an absent pulse, brooks of no delay in surgical treatment for restoration within six hours will usually be successful, whereas procrastination beyond this time is disastrous. At this operation, after dealing with soft tissue and bone damage, the fascial compartments of the limb are opened widely to release the swollen muscles, blood clot, and the collaterals; and then the vessel itself is examined.

Arterial spasm, if present, is relieved by the local application of 4 per cent. papaverine (Kinmonth, 1952). In a major artery, thrombosis, with or without actual separation of the tunica adventitia, is treated by excision of the involved segment up to healthy vessel at either end, after which continuity is restored either by direct suture or through the intermediary of an arterial or autogenous vein graft. Smaller vessels are carefully divided above and below the injury, taking care to avoid important collaterals.

Surgical exploration of an arterial aneurysm or fistula is deferred if the swelling is not excessive and the circulation is not endangered, as the results of interval treatment are excellent (de Bakey and Simeone, 1946), and arrangements more favourable to successful reconstruction can be made at this time.

In 5 cases of acute or subacute injury admitted to the Cardio-thoracic Unit, two involved the popliteal artery, one the common femoral, one the superficial femoral and one the subclavian. Arterial continuity was effected in all and satisfactory results achieved.

The problem of thrombosis secondary to minor trauma is considered with degenerative arterial disease.

(3) *Embolism*

The immediate objective, namely to restore a circulation beyond the occlusion adequate to prevent muscle ischaemia and gangrene, is attained by general measures to improve the cardiac output and blood presure as well as by local attention to the obstruction, the collateral circulation and the prevention of secondary thrombosis. Urgent embolectomy, often under local anaesthesia, is the treatment of choice in most cases (Jepson, 1955) especially for embolism of the cervical course of the carotid arteries, the subclavian-axillary artery, the aortic bifurcation, the common femoral and the popliteal arteries, provided the general outlook warrants it, the time interval is not unduly long, and facilities are available.

In later cases, if retrograde flow can be achieved by sucking out the loose branching peripheral propagated clot, excision and grafting of the site of infarction may prevent secondary thrombosis.

Of 21 cases of acute peripheral systemic arterial embolism admitted to the Green Lane Hospital over the decade 1946-1956 and treated surgically, 14 were associated with cardiac failure or infarction at an average age of 74, four were associated with rheumatic valvular disease at an average age of 43, two occurred from bacterial endocarditis (one of these a late sequel to a Blalock operation for Fallot's tetralogy) and one with an abdominal aneurysm. Ten of these cases (50 per cent.) died in hospital, mostly from grave general disease and not from the embolism, which threatened only the limb. Of 3 deaths associated with rheumatic mitral disease, multiple emboli were present in two, and a superior mesenteric embolus with gangrene of the bowel in the other. Of the 6 deaths associated with degenerative heart disease or infarction, coronary occlusion was responsible in four, surgical shock in one, and multiple emboli in one. In 12 cases which survived recovery of the limb followed embolectomy in nine (aortic bifurcation 1, common femoral 5, brachial 3) and excision of a mycotic aneurysm at the site of impaction in one. Amputation was necessary in the two unsuccessful cases involving the common femoral bifurcation and the popliteal arteries respectively.

In a recent survey by Jepson (1955) the incidence of peripheral gangrene following unrelieved embolism of the arteries to the lower extremity, according to site, was: aortic bifurcation 50 per cent., iliac 60 per cent.,

common femoral 50 per cent., superficial femoral 30 per cent., popliteal 10 per cent. The patient mortality was 39 per cent. and most of the survivors had symptoms of intermittent claudication.

The distribution of emboli and a comparison of the results of surgery and conservative management was studied in 200 patients by Warren, Linton and Scannell (1954). The lower limbs were affected in 76 per cent. of cases, and the circulation was restored without gangrene in 86 per cent. treated by embolectomy as compared with 60 per cent. treated non-operatively, the hospital mortality in both series being 35 per cent. and accounted for by the primary disease rather than by embolism.

(4) *Degenerative arterial thrombosis*

As segmental thrombosis is usually a local manifestation of generalized and progressive arterial disease with a grave prognosis, the axial arterial obstruction is ignored in these cases and management in accordance with a diminished expectation of life practised (Learmonth, 1940). In general lumbar sympathectomy has been found both to increase the diameter and flow through the collaterals and to dilate the vessels of the skin, thereby improving the nutrition to the limb and preventing gangrene. In some cases, especially those with an occlusion more centrally situated, the collateral return to the major vessel has been improved and, with it, the claudication distance (Learmonth and Slessor, 1952; Boyd, 1949) but more frequently remains unrelieved.

Of 12 cases of acute and subacute peripheral arterial thrombosis admitted to the Green Lane Hospital (1946-1956) with grave ischaemia not submitted to reconstructive surgery, and occurring at an average age of 61 years, 5 died in hospital and 7 recovered. The limb was saved by lumbar sympathectomy in 4 while amputation for gangrene was performed in three. If these figures are compared with 817 cases of coronary thrombosis (252 died) and 117 cases of cerebral thrombosis (33 died), admitted during the same period, the relatively minor role of the peripheral vascular problem (especially the surgical one) and the overwhelming selectivity for the central and vital areas is apparent.

In cases with lesser degrees of ischaemia, at the initial complaint of claudication a short segmental thrombus with a satisfactory main vessel beyond can usually be demonstrated by arteriography (Mavor, 1956). As

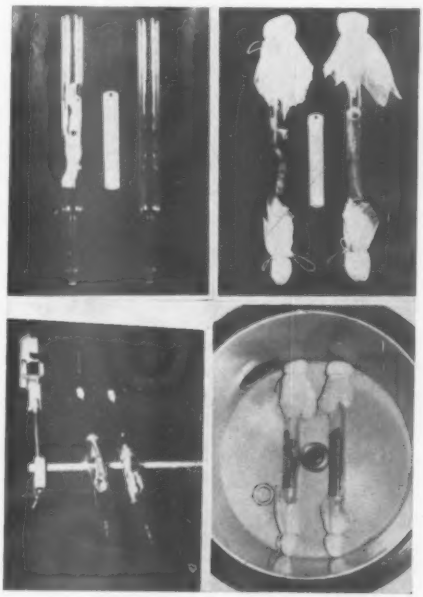


FIG V. Photographs of the method of arterial preservation described.

(a) Artery in special soft glass container.

(b) After replacement of sterile protectors.

(c) Grafts and containers in the container of the Edwards freeze drier.

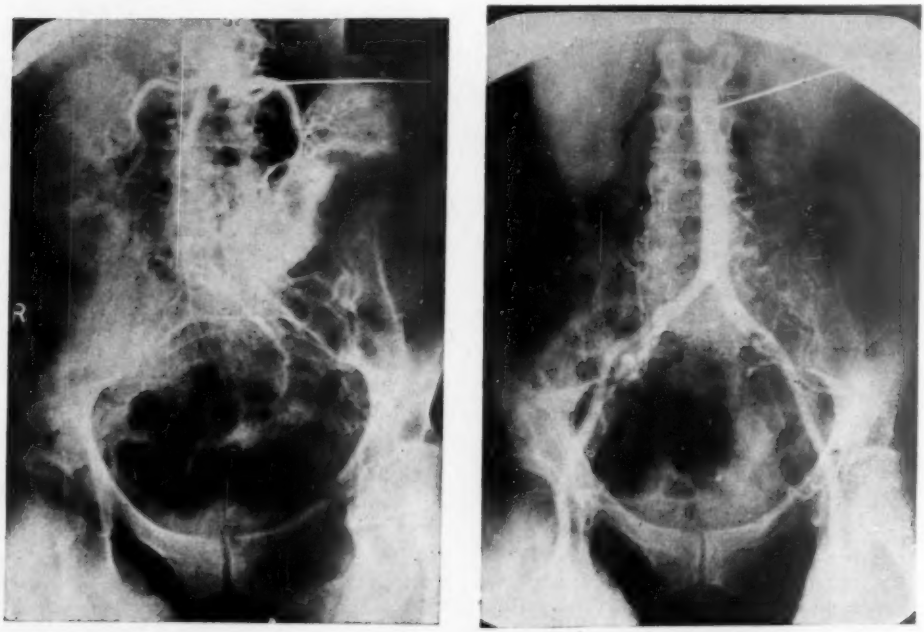
(d) Secondary drying after sealing the large end and drawing out the other which has been fashioned to fit the nipple of the Phillips freeze drier.

the type of disease and the extent of secondary central and peripheral thrombosis cannot be predicted it is reasonable to advise this examination in all early claudicants without grave disease and to treat localized obstruction at this stage in suitable cases without general obliterative arteritis, by restoration of the axial flow at a time when the peripheral bed allows a good run off from the arterial bed rather than waiting until later when this is not so. Endarterectomy or direct removal of a short thrombotic occlusion through a plane of cleavage in the tunica media (Dos Santos, 1947) has been followed by a high recurrence

rate and the method is now used only for localized lesions in the aorta and common iliac vessels (Rob, 1956). Excision and grafting has proved satisfactory for the great arteries extending to the pelvic outlet, but not beyond as there has been early thrombosis in the great majority (Rob, 1956). The insertion of an arterial by-pass to restore the axial flow (Crawford and de Bakey, 1955; Linton, 1955) which can be done with as little danger as a lumbar sympathectomy, by eliminating possible blind end anastomosis may provide a surgical solution for the immediate problem, while advancing knowledge concerning the aetiology of arteriosclerosis gives hope that the present gloomy prognosis may be confounded.

contaminated in 50 per cent. of cases. The grafts are placed in special ampoules, freeze dried in the standard sealed-in vacuo freeze drier, and stored at room temperature (Fig. V) (Nicks, 1956).

The grafts have been shown to function in the body as inert tubes, the endothelium growing only a few centimetres from either end, the intervening gap being lined by layer composed of fibrin, flattened fibroblasts and collagen. These vessels, so easily prepared and stored by the method described, are universally suitable and although degenerative changes do occur, they have not been harmful. The technique preserves the inner surface and the elastic tissue without much damage to its



(a) (b)

FIG. VI. (Case 6) E.C., 70 years. Aortic thrombosis. Aortic bifurcation graft. Aortograms showing:
(a) Thrombus extending up to the renal arteries. The distal extension is not demonstrable.
(b) Post-operative reconstruction of the aorta.

ARTERIAL REPLACEMENT FOR DEGENERATIVE DISEASE

In this Unit nearly all the grafts taken in the operating theatre have been sterile whereas those taken in the autopsy room have been

physical nature. It seems likely that homologous arteries, evolved and streamlined by nature, will continue to be used for long grafts inserted into smaller vessels in which a smooth lining and elastic recoil are important in maintaining a constant flow.

For larger vesels, especially in communities where grafts are not readily available, plastic prostheses of Orlon, Vinyon N and Nylon have all proved satisfactory. Initial trial of the soft, easily workable polyvinyl sponge, from which a prosthesis can be moulded and sterilized in boiling water for each individual case (Rob, 1956) has been promising, and this is being assessed in our surgical laboratory.

During the operation the blood pressure and the circulatory volume are maintained as a prophylaxis against coronary thrombosis.

The grafts are reconstituted in heparin saline and regional heparin (20 cc. of 0.06 per cent.) delivered into the peripheral end of the artery during the period of clamping but this has not been used systemically after operation for the past two years.

Grafting, both by direct reconstruction and a by-pass has been performed for degenerative thrombosis in the following situations: the aorta (2 cases) (Appendix Case 6, Figs. VIa and VIb), the common iliac artery (3 cases), the superficial femoral artery (8 cases). Grafts in the aorta and common iliac artery have been successful but in the femoral artery the results have so far been unfavourable, one case dying from coronary thrombosis, two developing thrombosis in the graft immediately afterwards, one a short time later and requiring amputation, and another after eight months, following a careless injury sustained while driving a bulldozer, which has recently been restored by a further long by-pass graft (Case 8). Three other cases are well (two with a by-pass).

The results in the peripheral arteries will have to be reassessed in the light of the by-pass operation and if the preliminary favourable reports are sustained (Crawford and de Bakey, 1955), the scope for arterial grafting may be widened to include suitable patients with threatened or early established gangrene (Case 9, Fig. VII).

SUMMARY

Some of the basic pathological problems in connection with the surgery of defined types of major arterial obstruction are discussed.

The results of surgical treatment at Green Lane Hospital of cases with congenital, traumatic, embolic and degenerative obstruction is recorded and discussed together with a table of statistics of wounds involving arteries of the New Zealand Armed Forces.

FIG. VII. (Case 9) S.M., 53 years. Local amputation performed and wounds healed rapidly. Gangrene of right toes following obliterative femoral thrombus. Foot immediately after graft from external iliac to popliteal artery showing venous filling.

ACKNOWLEDGEMENTS

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The operations referred to in the text have been performed by Mr. Douglas Robb and myself.

APPENDIX

Case 1

F.E., aged 45 years. Diagnosis: Popliteal aneurysm sequel to disruptive injury at the knee joint.

The patient's symptoms began a year previously following a severe extension injury to the right knee joint, at which time the leg was deeply bruised and swollen. Six months later he developed a swelling behind the knee which has enlarged progressively and caused severe pain and progressive flexion deformity at the knee joint. At clinical examination there was a popliteal aneurysm the size of a small apple. The only other interesting feature was hypertrophy and clubbing of the toes in this foot. A right femoral arteriogram (Fig. IIa) showed the ends of the popliteal artery to have been severed by the original injury and to open into an aneurysmal sac. A lumbar sympathectomy was performed on 23rd July, 1953, by Mr. Donald McKenzie to improve collateral circulation to the foot. Two weeks later the aneurysm was explored, tributary vessels controlled with coarctation clamps and an autogenous vein graft, nine inches long, inserted between the severed ends. The graft had been prepared at the commencement of the operation by excising the saphenous vein of the same leg and preserving it in heparin saline. The upper end was marked with a stitch and the graft was reversed on insertion so that this upper end was joined to the lower end of the artery and rendered the valves of no consequence. On completion the vein graft was the size of the popliteal artery and transmitted a normal pulse, and was supported in the belly of the gastric muscle. No anticoagulants were given. Convalescence was uneventful.

Six weeks later he had a normal arteriogram and could straighten the knee without pain. The unilateral clubbing had largely disappeared and he was back at work, very pleased with his operation. An arteriogram repeated on 8th October, 1954. shows an entirely satisfactory graft without dilatation (Fig. IIb).

Case 2

J.M., aged 67 years. Diagnosis: Superficial femoral artery thrombosis following trauma and atherosclerosis. Arterial by-pass graft 16th May, 1956.

He was butted by a cow in the mid-thigh four months previously and on the following day developed pain in the calves. The symptoms gradually improved over the next six weeks but at this time the toes became infected and he developed gangrene.

On admission the foot was dark and swollen and no pulse was palpable at the ankle. The arteriogram (Fig. IIIa) showed a well-developed collateral circulation with complete thrombosis of the superficial femoral artery extending from the bifurcation to the popliteal.

Following lumbar sympathectomy the colour of the skin was improved but there was still rest pain and coldness of the toes.

Operation: An arterial by-pass using a double length freeze dried artery was inserted from the common femoral artery above to the middle of the popliteal below. Following this there was a return of the pulses to the foot, healing of superficial gangrene of the toes and cure of the claudication. When he became ambulant claudication in the right leg only was noticed for the first time and the arteriogram showed a small segmental occlusion (Fig. IIIb).

Comment: Improvement of the skin nutrition only but not of the muscular pain followed sympathectomy and this was relieved only by restoring the axial strain. The development of thrombosis of the right femoral artery during convalescence is in accord with the major role of stasis and diminished flow in precipitating intravascular clotting in atheromatous vessels.

Case 3

S.M., aged 42 years. Diagnosis: Arteriovenous aneurysm of the right femoral artery following rifle shot injury. Excision of aneurysm followed by vascular insufficiency 5th April, 1950.

On admission he complained of shortness of breath on exercise of ten years' duration, and black-outs for two or three years. Following injury by a .22 rifle bullet in the groin twenty-seven years previously, which had been removed from the femoral vein, he had been increasingly short of breath on exertion.

On examination there was a marked pulsation and thrill in the right groin, which could be obliterated by local pressure, but no visible aneurysm. The right leg was half an inch shorter than the left. The heart was enlarged, the apex being in the 5th space four inches from the midline. The sounds were normal apart from numerous extrasystoles. The blood pressure was 160/50 mm. of mercury. X-ray showed increased intra-pulmonary markings and concentric enlargement of the left ventricle.

Operation: Following ligation and excision of the arteriovenous aneurysm the post-operative condition was without complication but his exercise tolerance was severely limited by claudication and fatigue in the right leg. On examination the heart size and the electro-cardiograph had returned to normal but the foot was distinctly colder than the left. A lumbar sympathectomy was performed but gave little relief to the claudication. An arteriogram on 20th August, 1956, showed interruption of the external iliac artery and an anastomotic circulation carried on through the internal iliac and deep femoral artery. The lower end of the superficial femoral artery was not visible and exploration showed this had become obliterated as far as the adductor opening.

Case 4

N.M., aged 61 years. Diagnosis: Thrombosis of the internal carotid artery. Resection under hypothermia. Death, after initial recovery, from arteriosclerotic thrombosis of the basilar artery.

He was referred from Dunedin Hospital (Professor Iverach) suffering from left homonymous hemianopia, brilliant optical illusions and diabetes. Minimal neurological signs present were indicative of a lesion involving the right temporo-occipital region of the cerebrum and the cerebellum, possibly thrombotic in nature. A cerebral angiogram demonstrated partial occlusion of the right carotid artery at its origin and of the peripheral part of the right posterior cerebral artery (Fig. Va and Vb).

Operation: 30th January, 1955. Resection of the internal carotid segment was undertaken at the patient's earnest request in an attempt to save the rapidly deteriorating vision, on the basis of it being due to the release of small emboli or to diminished circulation. The temperature was lowered with circulating ice cold water in a special blanket to 86.5°F, at which time he was removed to the operating theatre and the localized constriction (1 cm. long) at the origin of the common carotid artery excised and the open ends reconstituted by direct anastomosis, the time of circulatory interruption being twenty-four minutes. The temperature was allowed to recover spontaneously and he regained consciousness in six hours at which time there was a slow atrial fibrillation of the heart. Some hous later he developed dysarthria and lapsed into coma. There were neurological signs of a brain stem lesion from which he died thirty hours after the first operation.

At the post-mortem (Dr. S. Williams, 31st January, 1955) there were small areas of old infarction in the right occipital lobe and recent infarction involving the pons, cerebral peduncles, thalami and the anterior part of the cerebellum associated with thrombosis of the basilar artery which, together with both vertebrals was greatly narrowed and atherosclerotic. The right internal carotid artery was patent and there was a neat suture-line at the operation site. The cause of death was cerebral infarction due to thrombosis of the basilar artery and widespread generalized atherosclerosis.

Comment: The widespread nature of the atheroma in the post-mortem findings is in accord with known facts and is a warning against major surgery when suspected.

Case 5

C.F., aged 47 years. Diagnosis: Fracture dislocation of the knee with rupture of the popliteal artery. Successful arterial reconstruction.

He was admitted to Middlemore Hospital in a shocked state a short time following crushing of the left leg between two trucks. There was a compound comminuted intercondylar fracture of the lower end of the femur with an oblique laceration across the upper and medial aspect of the popliteal space. The foot was cold and pale. There was no palpable pulse about the ankle.

Operation: 22nd December, 1951. The popliteal artery was found to be completely ruptured, the ends being retracted and sealed with clot. An arterial end-to-end anastomosis was performed after stripping the adventitia and trimming to healthy vessel on either end. On release there was a good pulsation.

As there were no post-operative complications apart from oedema of the foot the skin behind the knee was grafted fourteen days later and later arthrodesis was performed by Mr. W. Pike. Follow-up report four years later by the patient states: "My leg gives no trouble and I walk for miles. I have long ceased using a walking stick and consider that I have two good legs, one stiff. I recently painted my house inside and outside with only a ladder to stand on for twelve to fourteen hours a day without difficulty."

Case 6

E.C., 70 years. Diagnosis: Aortic thrombosis. Aortic bifurcation graft.

She was well until eight years ago when pain in both hips developed insidiously after walking about 200 yards. This was promptly relieved by rest but the symptoms were evoked by less and less exercise so that two years previously she was unable to walk more than a few yards without resting. Suddenly at this time, after gardening one afternoon, she noticed severe pain in the whole of the right leg which persisted and prevented her taking more than a few steps. She was examined and treated for intractable arthritis. Eighteen months prior to admission she developed circulatory changes with numbness and coldness in the feet followed by patches of superficial gangrene in both feet for which she was admitted to Auckland Hospital where a sympathectomy was done in October, 1955 (Mr. D. McKenzie). The superficial gangrene healed but pain was unaltered. Over the nine months following this operation relief of pain was obtained only by hanging the legs over the side of the bed in which position she rested night and day.

Past history: She had smoked about 25 cigarettes a day for many years.

On examination: Blood pressure 180/80 mm. of mercury. She was in great misery with flexion deformities of the knees. The feet were cold but the nails were not deformed. There were no peripheral pulses. Aortogram showed complete thrombosis of the aorta extending right to the renal arteries (Fig. VIa).

Operation: 22nd May, 1956. The aorta was explored through a midline incision, the intestines being delivered into a polythene bag. The aorta was divided just below the renal vessels and the thrombus plugging the upper end cored out from below during which manoeuvre haemorrhage was controlled by finger pressure on the aorta above the renal vessels. The aortic bifurcation graft was inserted into this cuff from below the renal arteries to the bifurcation of the common and internal iliacs on each side, clot being removed by endarterectomy from each of these vessels until there was brisk retrograde bleeding. During the period of clamping heparin was injected into the peripheral vessels. On completion the pulses were normally palpable in both legs. The blood pressure remained fairly low for the next few days but convalescence was uninterrupted and six weeks later she had no pain and

could walk unaided with a stick. There was some residual swelling of the ankles probably due to the unusual amount of blood passing to the legs. The flexion contracture at the knees had completely disappeared and there was no claudication. The aortogram showed restoration of the aorta and iliac arteries (Fig. VIb).

Comment: The progressive and intractable nature of aortic thrombosis is well demonstrated and contrasts with the immediate relief by aortic replacement.

Case 7

S.M., aged 48 years. Diagnosis: Thrombosis of the aorta bifurcation and left common iliac artery. Excision of clot from the right and aorta-iliac bifurcation graft on the left.

This patient was admitted complaining of cramping pains in the left buttock of twelve months' duration, pain in the left leg on walking for eight months and wasting of the left leg muscles for five months. The discomfort was first noticed in the left buttock and posterior part of the thigh when sitting in his car and was relieved only by getting out and walking. Some months later the pain in the buttock and calves was noticed to be provoked by walking and became so progressively worse that on admission his claudication distance was scarcely fifty yards. These symptoms greatly curtailed his activity and threatened his livelihood as a pig farmer in hill country. He was of a long-lived family, was abstemious both as regards food and alcohol, and smoked about twenty cigarettes a day.

On examination he was a fit man and, apart from greying hair, showed no sign of degenerative disease. There was normal sensation in the left leg which, however, was colder than the right. Blood pressure 150/82 mm. of mercury. Arterial pulsation was palpable in the thigh but was markedly diminished at the ankle and there was one inch wasting of the left calf. General examination of the cardiovascular system was unremarkable apart from high blood cholesterol of 263 mgs. per 100 ml.

An arteriogram showed complete occlusion of the left common iliac artery extending from the bifurcation of the aorta but the lower end was not delineated.

Operation: 20th February, 1956. The common iliac and lower aorta were explored extra-peritoneally by an oblique lower abdominal incision. The thrombus was found to extend over the aortic bifurcation when the terminal aorta was clamped and opened. Clot had to be sucked from the origin of the right common iliac artery before retrograde bleeding occurred. An anastomosis was performed between the anterio-lateral aspect of the aorta one inch above the bifurcation and the external iliac artery just below its bifurcation as there was a good retrograde flow from the patent internal iliac artery taking origin just below the thrombosis.

Post-operatively a good pulse was felt at the ankle and follow-up shows complete relief of pain and claudication, and the aortogram showed a normal axial flow through the iliac vessels.

Case 8

D.J., 52 years. Diagnosis: Recurrent thrombosis of superficial femoral artery graft after injury. By-pass re-graft twice with success.

He was referred complaining of intermittent claudication of the right leg after walking for 100 yards for one year. The right foot was colder than the left and arterial pulsation, though palpable in the groin and the ankle, was diminished. There was no evidence of general cardiovascular disease and a right femoral arteriogram showed a segmental obstruction extending from the middle of the superficial femoral artery to the origin of the popliteal artery. There was no gross disease of the arterial system.

On exploration, 18th May, 1955, the thrombus was found to extend for fifteen inches from the origin of the deep femoral artery to the upper third of the popliteal space. This vessel was excised and replaced by a freeze dried graft and on completion there was a return of the usual pulse at the ankle. The symptoms were completely relieved and he lived a normal life for twelve months when he was re-admitted with claudication. Two days previously, while working with a bulldozer, he received a heavy blow directly on the subcutaneous graft in the thigh and later than evening he developed cramping pains in the leg. On examination the right foot was colder than the left and although the femoral pulse was present, it was absent at the ankle. A firm thrombosed vessel could be felt in the position of the graft in the thigh and was confirmed by an arteriogram.

After a trial of anticoagulants claudication at fifty yards presented and resection of a graft was agreed upon.

A repeat by-pass was performed on 19th June, 1956, between the common femoral artery and the mid-popliteal artery using two grafts joined together and leaving the thrombosed artery in place. Some hours later the foot felt cold and the leg was painful. The graft was felt as a solid cord under the skin. Immediate exploration was performed and the thrombosed artery was removed. At the lower end soft clot extending peripherally into the popliteal artery, was sucked out to allow retrograde bleeding from the patent lumen. The proximal end of this open popliteal artery did not bleed, but again, after sucking this out, bleeding was restored. A further freeze dried by-pass graft was inserted to replace the thrombosed vessel. Following this pulsation was restored to the ankle and convalescence was uninterrupted. A follow-up arteriogram shows the graft to be working satisfactorily and his symptoms are completely cured.

Comment: This was our only case of traumatic thrombosis in a graft. Thrombosis of the second graft was probably due to stasis occasioned by release of the upper clamp before the lower anastomosis was completed. This leg would certainly have been lost if urgent replacement had not been undertaken and peripheral propagating clot removed by suction prior to regrafting.

Case 9

G.M., 53 years. Diagnosis: Gangrene of toes from obliterative femoral thrombosis. Successful iliac-popliteal by-pass arterial graft.

Gangrene of the left fifth toe two years previously at which time he was found to be diabetic and received continual supervision. Six months before admission he complained of intermittent claudication of both calves followed in four months by gangrene of the first, fourth and fifth toes.

On examination the femoral pulses were present on both sides but pulsation was absent at the knee and ankle. The circulation to the skin was much impaired especially on the right side and the toes were gangrenous. A bilateral femoral arteriogram showed complete thrombosis of the right femoral artery with a good popliteal artery below and a rather worm eaten, though patent, arterial system on the left side. The skin condition was significantly improved by bilateral lumbar sympathectomy but rest pain in the right leg and foot remained. An arterial graft was advised and accepted.

Operation: 16th August, 1956. An external iliac-popliteal subcutaneous by-pass graft using two freeze dried arteries sutured end to end was performed. On release of the clamps there was good pulsation in the distal popliteal artery. The wounds were sealed with nobecutaine and drained for twenty-four hours after which time they were left open to the air. The operation was covered with chloromycetin as the foot was infected with a coagulase positive staphylococcus.

The post-operative course has been satisfactory with complete return of the distal pulses and such a good circulation that local amputation was performed and healing accomplished without incident.

Comment: A mid-thigh amputation was inevitable without this graft which was undertaken with some apprehension in the presence of diabetes and a coagulase positive staphylococcus infection.

Case 10

C.H., aged 51 years. Diagnosis: Traumatic obstruction right femoral artery.

He was admitted six weeks after ligation of the right femoral artery in mistake for the saphenous vein. Following the operation there were symptoms of coldness and swelling of the leg, ankle and foot. On admission there was a complaint of numbness below the knee and tightness in the leg although the claudication distance was difficult to assess.

On examination there was a strong femoral pulse at the inguinal ligament but none in the popliteal region or at the ankle. There was no wasting or swelling but the leg felt colder than its fellow.

An arteriogram revealed complete occlusion of the femoral artery above its bifurcation and filling of the deep femoral and superficial femoral by varicose collaterals.

A freeze dried arterial by-pass graft was inserted between the common femoral and the superficial femoral arteries some seven inches blow the obstruction. The post-operative course was uneventful. The pulse had returned at the ankle and the symptoms were almost entirely relieved.

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SECTION-CUTTING OF UN-DECALCIFIED BONE

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THE modern surgeon has many advantages over those of 50 years ago. He is able to diagnose, with ease and certainty, minor variants of complex conditions in a way that would have astonished his predecessors. This has been achieved partly by continuous clinical study and assessment during several decades, but also by the application of information supplied by those specialists who have delved in different but related fields. Now, with the help of the radiologist, he is able to distinguish such conditions as melorheostosis, Milkman's syndrome or polyostotic fibrous dysplasia. He does not hesitate to diagnose or at least suggest the presence of an osteoid osteoma, eosinophilic granuloma or simple bone cyst. These conditions have been observed, differentiated and named by the pathologist—in many cases thereby possibly avoiding the unnecessary removal of a limb and certainly providing a more accurate and comforting prognosis for the patient.

Such progress has been made possible by improved techniques of tissue examination in addition to careful, thorough and more numerous observations.

Investigation of bone structure has always presented some difficulties because of the calcium-salt content which has rendered sectioning troublesome and awkward. The calcareous material damaged the knife edge, and broken and scored sections of tissue resulted with corresponding diminution in value for study. In consequence it became the routine practice to remove the calcareous material chemically. Histological sections, as good as those of other tissues, were then obtained but the details of cellular structure were likely to be lost or altered and the distribution of calcium salts was not demonstrable. The necessity for sections of un-decalcified tissue was recognised early and many attempts have been made to produce these. One method, for example, was by sectioning or grinding bone by means of a rapidly rotating wheel, but such methods produced sections of 15μ thickness. These provide valuable information but are unsatisfactory for many of the finer observations which present-day investigations demand.

The details of technique belong to the realm of the histologist, but its application is of importance to the orthopaedic specialist, in so far as much of the material for study must come from the operating theatre, and the results of such study may add to our knowledge of the conditions for which operation is performed. It is with this justification that an account of such investigations is given here.

The failure of the standard paraffin section of de-calcified bone to give an adequate picture of normal or pathological bone histology has long been a matter of concern to those interested in this subject. The many attempts made to obtain a true representation of bone structure, mainly using ground sections, have required a great expenditure of effort for very little reward and have never become routine. As mentioned, sections thin enough to compare with the paraffin sections of other tissues have not been achieved. A method to provide sections of 10μ or less which are free of shrinkage and distortion is highly desirable to help our understanding of bone structure in health and disease.

It is well known that embryonic bone or lightly calcified osteoid has been cut successfully without decalcification but the method here described is equally applicable to the normally calcified bone of adult tissues.

Evolution of the Method

One of the principal reasons for failure of routine methods of sectioning is that areas of unequal hardness are presented to the cutting edge of the knife. In order to cut material as hard as bone it is necessary to embed it in a substance of equal hardness. Paraffin wax is of course unsuitable but the application of the acrylic plastics has provided a range of materials of varying hardness which is ideal for the purpose. The hardness of the block can be adapted to the type of bone it is desired to section. At first it was thought

that the normal microtome knife would be unsuitable for cutting this material and so glass knives, similar to those applied to section cutting for the electron microscope, were used. This imposed a serious restriction on the size of the block and, although successful, was discarded as impractical.

A heavy duty steel knife was tried with such success that it has now become standard practice. Few limitations are imposed by its use and all but dense cortical bone can be successfully cut.

FIG. I

FIG. II

FIGS. I and II. High power photomicrographs of a section of un-decalcified bone to show individual osteocytes as found in normal bone. The cell is not shrunken and the radiating cytoplasmic processes are clearly demonstrated. Alizarin with phosphomolybdic acid stain. (x 1200)

This work confirms the findings of Woodruff and Norris (1955); the techniques were elaborated and the results were arrived at independently. The present method is the same in principle but somewhat simpler in application and is more suited to routine laboratory practice.

METHOD

1. The specimen is dehydrated in the usual manner by taking it through graded alcohols to absolute alcohol. The time of each stage will vary with the size of the block of tissue, but is usually eight to twelve hours.

2. It is immersed in 50 per cent. alcohol, 50 per cent. monomer overnight and then placed in 100 per cent. monomer. The monomer usually consists of 10 per cent. methyl methacrylate with 90 per cent. butyl methacrylate, 2 g. per cent. benzoyl peroxide is then added as catalyst.

3. The specimen is orientated for cutting in the vessel in which polymerization is to take place; the mixed monomer containing catalyst is poured over it, allowing sufficient quantity for a reduction in volume due to evaporation of the monomer; the vessel is placed in an ultra-violet light chamber. Large gelatin capsules of the type used in veterinary therapeutic work have been found to be very convenient for the purpose. During polymerization, bubbles are likely to form in the acrylic. These can only be avoided if the process is slow and, if they begin to appear, polymerization should at once be temporarily stopped.

The time of polymerization will vary with the size of the specimen and is usually between eight and thirty-six hours.

4. Each block is prepared for cutting by grinding down to the face of the section and then polishing on a buff. The gelatin (of the capsule) is stripped from the edge and the block is then ready for cutting.

5. The block is held in a screw clamp adaptor which will fit a standard microtome such as Leitz or M.S.E. A heavy duty knife is held at an angle of 80° and cutting proceeds in the normal fashion.

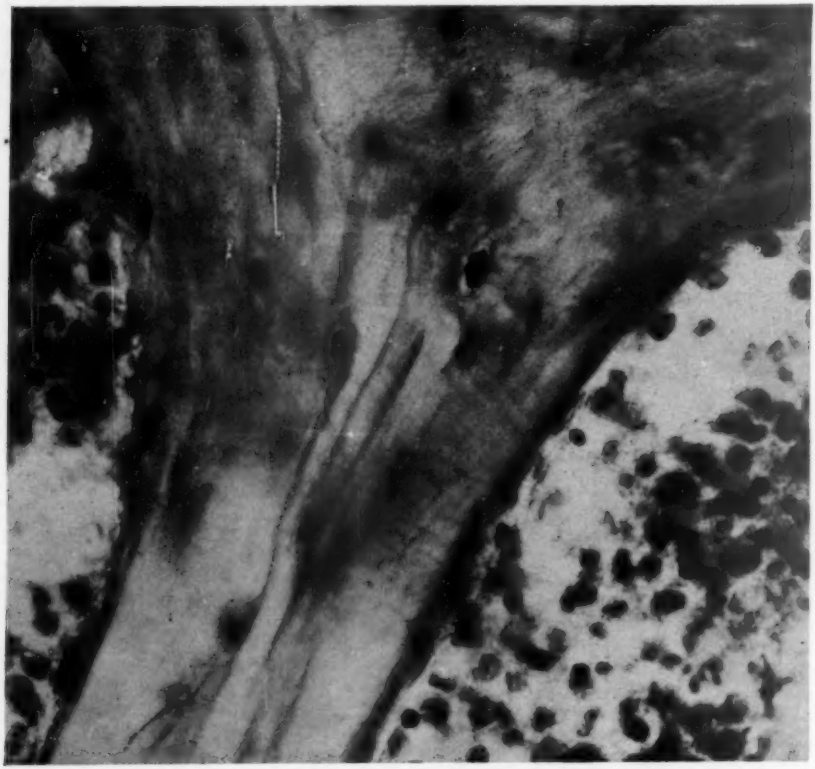

FIG. III. Photomicrograph of an 8u section of a bone trabecula from a vertebral body. The longitudinal lines indicate collagen bundles. The darker staining immature calcium deposits in relation to these and to the osteocytes is a constant feature. Haematoxylin eosin stain. (x 750)

6. Sections can be cut as thin as 5μ but it has been found easier to cut at 8μ, at which thickness the general standard of material is better. When cut, the sections tend to roll into a tight spiral which may be very difficult to unroll and flatten. However, this may be overcome in one of two ways: first, by grasping the leading edge of the section with fine forceps and thereby transferring it to a water bath at 50°C when it will uncurl and flatten, and secondly, wetting the knife may prevent a tight spiral, a water bath then unrolling it completely.

As the section dries on the slide it is liable to curl at the edges and later may lift during staining. To prevent this, gelatin 2 per cent. to 4 per cent. is added to the water bath.

7. The slides are dried in a 37°C oven for four hours and are then ready to have the polymer removed before staining. This is achieved by immersing them in either chloroform or carbon tetrachloride for a minimum of twelve hours. The more rapid solvents such as ethylene dichloride or methylene chloride distort the section and often cause it to lift.

8. The section is dried, cleared in xylene, and stained in the usual way. So far staining of the material has been by haematoxylin and eosin, and alizarin (Cameron, 1930) has also been tried. There is, however, no reason why any of the recognized histochemical methods could not be used on this material, and these are being studied.

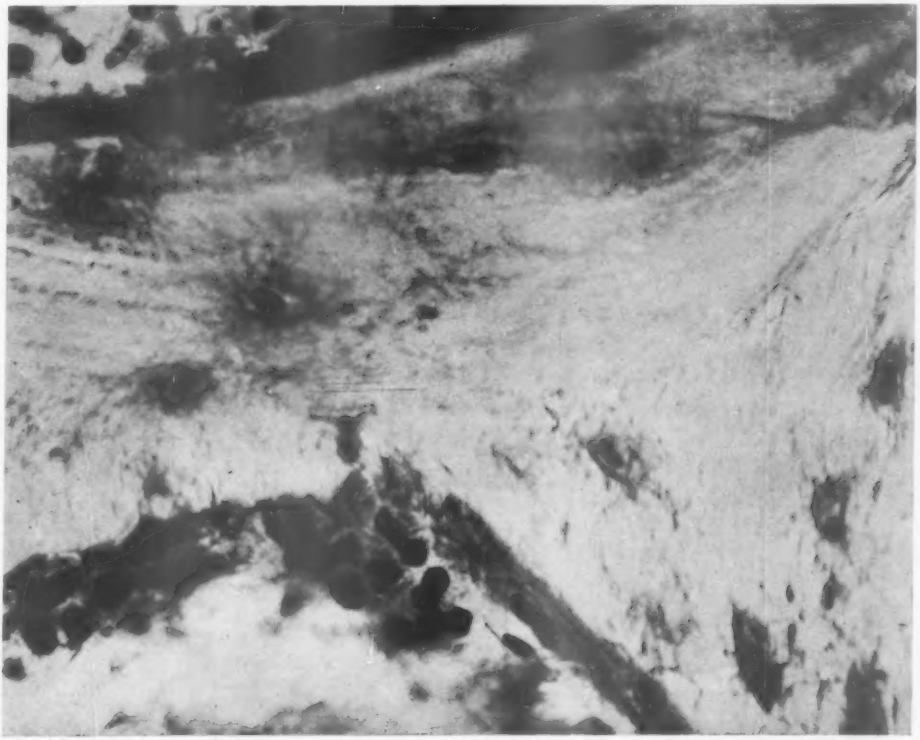

FIG. IV. Photomicrograph of an 8u section of a bone trabecula from a vertebral body. The granular nature of the calcium deposits is obvious along the collagen bundles, round the osteocytes and in the peripheral osteoid layer. The radiating protoplasmic processes from osteocytes can be observed in the haematoxylin eosin section. Haematoxylin eosin stain. (x 750)

RESULTS

The sections are not always perfect when observed with a scanning lens as they are not completely flat and have a slightly wavy appearance in the marrow. If the marrow is cellular the cells are liable to become loose and float over to obscure the bone trabeculae; this is a technical problem that will probably be overcome in due course. However, examination under high power is most rewarding. Protoplasm is not shrunken and bone cells completely fill the lacunae. Their radiating processes can be seen in the haematoxylin and eosin section and are very well seen in the alirazin section differentiated with phosphomolybdic acid (Figs. I and II).

The bone structure of these sections is of special interest. Mature stable bone stains evenly with eosin and the fine longitudinal striae of collagen bundles can be seen well. Along the arrest lines, around the osteocytes and at the margins of the trabeculae there is a granular stippling which stains with haematoxylin (Figs. III, IV and V). This granularity probably represents immature bone, as it is seen on the side of the trabeculae where bone is being laid down and is absent on the side of bone resorption. At the sites of active deposition the granules are larger than elsewhere (Fig. V).

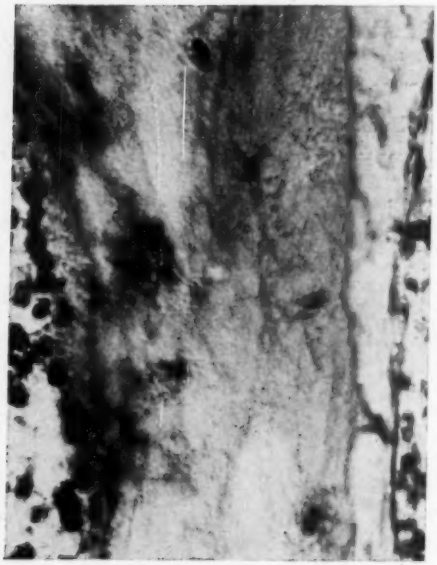

FIG. V. Photomicrograph of an 8u section of a bone trabecula clearly showing the particulate nature of the calcium salt deposit on the osteoid border of the trabecula. The right side edge does not show this and probably implies that the bone is "inactive" in this area. Haematoxylin eosin stain. (x 750)

These appearances have been constant in the material so far examined but require confirmation on a wider range of normal and pathological bone and are the subject of further study.

SUMMARY

A method of obtaining histological sections of bone which has not been decalcified is presented. The method is applicable mainly to cancellous bone but can also be used on cortical bone which is not too dense. The importance of this method in the understanding of normal structure and interpretation of pathological conditions is well recognized and a brief account of results already obtained is given, with representative photographs to illustrate these.

ACKNOWLEDGEMENTS

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THE SURGEON AND RESEARCH TODAY

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"Nothing has such power to broaden the mind as the ability to investigate systematically and truly all that comes under thy observation in life."

—Marcus Aurelius: *Meditations.*

A REVIEW of the works of the early surgeons shows that, generally, in addition to the assemblage of the various stores of knowledge of his period, he presented his own observations in detail. These, of course, always depended in some measure on the former and fell into two main groups: the different types of treatment which he had found satisfactory in dealing with various conditions and observations on the characteristics of the diseases themselves. For the most part, these last were clinical observations and those made either post-mortem or in the late stages of the disease. Nevertheless, many of these early investigators showed considerable clinical acumen, keen observation and remarkable judgment and they all provided some component, large or small, of the fabric of our present-day knowledge.

A most important feature of the work of these surgeons is that it was recorded. Had this not been so, it is certain that we would now have no knowledge of them or of their work and it is probable that there have been many, as great as these with whom we are well acquainted, who are unknown to us either because they did not record their observations or their records have been lost. It is probable that the former was usually the case because it is remarkable how fragments of lost manuscript have come to light even many centuries after they were written and apparently lost. It has been said that the difference between pre-historic man and his modern descendant is merely that civilized man records his observations and ideas and these are thus available to his successors even in the absence of direct communication. The importance of this should be self-evident in our modern life but, curiously enough, its significance and personal application is not always appreciated by those making observations.

Surgery advanced very slowly and then rather more rapidly in the early part of the nineteenth century, in common with other activities, as a result of the general social and economic changes of the period. Then, just less than 100 years ago, the remarkable revolution, which is still influencing our thought and activities, occurred.

This was the direct result of the rapidly increasing knowledge of chemistry and the application of physical laws which gave such advances as the development of the achromatic microscope. The discovery and production in quantity of substances which became the antiseptics on the one hand and the discovery of bacteria on the other made possible the introduction of the antiseptic, to be followed by the aseptic, era.

A further application of the microscope to the study of tissues of animals demonstrated details of structure which had previously been unknown and this method of investigation was soon applied not only to the normal but to various forms of abnormal conditions.

Morbid Anatomy

This, as it affects the surgeon, is frequently referred to these days as surgical pathology. Attention was given at first to the examination of tissues removed from the body after death and a perusal of the literature of the end of the last century shows the tremendous amount of material that was examined and the enthusiasm with which investigations were carried out. Most of even the rare conditions, and some which today are regarded as novel, were actually first seen and quite well described during this time even though often their nature was not understood. As more attention was given to the elucidation of individual diseases the necessity for precise and

more detailed information on cellular structure was appreciated and it was found that this was very often not satisfactory in tissues examined at post-mortem. The difference in appearance between these and the tissues of animals examined immediately after death in the laboratory was obvious and the desirability of examining material removed at operation gradually became accepted. At the same time, doubtless because most clinicians had not had adequate laboratory training, tissues were not fixed at a reasonably early stage after removal from the body and indeed it has taken several decades for the necessity for this early fixation of material to be generally realized. A comparison of the histological appearances of tissues fixed immediately and fixed after periods during which autolysis could occur showed the remarkable differences that would sometimes be seen and thus the misleading observations which could be made as the direct result of autolytic changes due to delayed fixation.

Many valuable observations of the gross appearances of conditions, which provided much significant information on the early stages and the life history of these conditions, were made and the literature contains a wealth of information derived from surgical material. These observations were the necessary precursor of subsequent functional studies. At the same time histological details were often ignored and, in certain cases, the gross observations were correspondingly vitiated.

Although complete investigation of material removed at operation is still not universal, such routine examination is generally regarded as one of the essential criteria of efficiency in a surgical unit. The information is examined from two points of view: (1) as a check on the clinical and pre-operative diagnosis of the condition and (2) as a method of furthering knowledge of the disease. These, at first sight, are apparently quite distinct and different; they are commonly regarded as completely dissociated. However these two viewpoints are closely inter-related and indeed are really two facets of the same proposition—that important deductions may be made from carefully collected information. The principle that the immediate and the remote significance of observations are but different values to be placed on conclusions derived from the same phenomena should never be forgotten, that is to say, that information gained for the immediate purpose of diagnosis may be well employed in adding to general knowledge of a condition.

The emphasis on the importance of placing tissue in an adequate fixative at the earliest possible moment has sometimes led to the loss of valuable information where the nature of bacteria causing an infection was important but not ascertained; this error in turn has led to an inhibition regarding early fixation of tissues. The obvious solution, the segregation of a piece of tissue before fixation of the main specimen or the division of the tissue, for example a lymph node, into two equal parts, does not merit special discussion. The essential thing is that a sufficient amount of attention should be given to these details which are of paramount importance in the production of satisfactory material for the diagnosis and study of the particular condition.

Proper preservation of a tissue or organ often demands the technical procedures of perfusion of vessels, filling of cavities with fixative or pinning out of specimens and such must be done by individuals other than the surgeon and his assistants who necessarily proceed with their operation. At the same time, if the observations on the material are not adequately integrated with the clinical information, much valuable knowledge is lost; this is apparent in many of the papers which appear on surgical pathology. On the other hand, the information which can be obtained by the prompt and appropriate treatment of specimens is itself evidence of the value of attention to this. When the surgeon or an assistant displays an active interest the results are most rewarding, not only from the point of view of information obtained but also from that of specimens which are a credit to any museum and are thus of great value in teaching.

Digestion and autolysis of the epithelium lining parts of the alimentary canal commonly prevents satisfactory observation of this tissue in post-mortem material but in adequately treated post-operative material satisfyingly preserved mucous membrane is the rule. An example of one organ which gave much trouble for a considerable time (and sometimes still does) is the gall bladder. Loss of the superficial epithelium was so common that it was regarded as the normal state but

if the organ is opened or the cavity injected with fixative beautifully preserved mucosa will be found.

Tissue of the central nervous system also presents difficulties because it is relatively impenetrable to fixatives. This was found recently to be a problem in the investigation of monkey nervous tissues in relation to the testing for poliomyelitis vaccine and special precautions had to be taken to ensure that small pieces of tissue were fixed as early as possible.

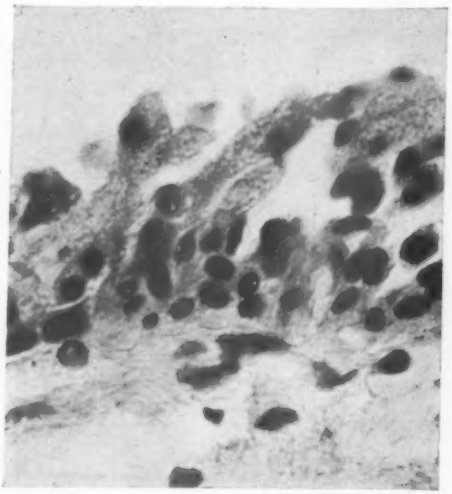


FIG. I. Photomicrograph of a section of synovial membrane showing stratification of the lining cells. The fine vacuolar character of the superficial cells is well preserved. (x 420)

A technique, which is becoming generally used and overcomes many of the problems of early tissue fixation, is the punch or needle biopsy. It has certain limitations such as, for example, some uncertainty that an appropriate area is chosen but the advantages easily outweigh any disadvantages.

The chemical which has come to be the most commonly used fixative is formaldehyde (4 per cent. formaldehyde or 10 per cent. formalin) and is of special value because of its remarkable penetrability and the speed with which it permeates tissues. Various other substances, particularly salts of the heavy metals (for example, mercuric chloride), have special virtues but it is probable that formalin will remain the routine fixative for tissues obtained at operation because of the characteristics mentioned above.

The surgical team must be sufficiently interested in and aware of the technical problems if full value is to be obtained from the tissue removed. The specimen should not be allowed to remain in a container in a warm operating theatre for long periods (waiting until the operation is over) nor should there be any delay in its removal after the blood supply has been cut off. If attention is paid to these details excellent results can be obtained (Figs. I and II).

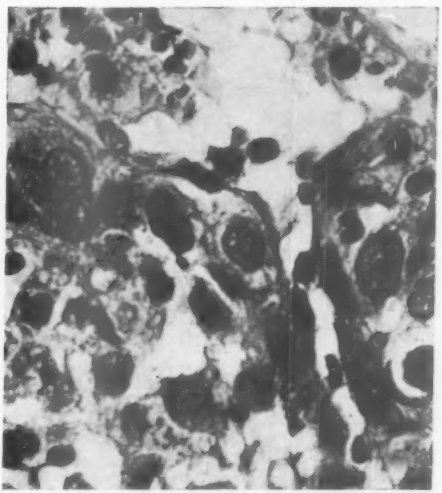


FIG. II. Photomicrograph of a section from a bone tumour biopsy. The cellular and nuclear detail is good. Formalin fixation. (x 480)

Many investigations require special technique to demonstrate particular cell components or inclusions. Special fixatives for the study of such may be used quite satisfactorily provided the tissue is placed in the appropriate solution expeditiously, or in some cases, dealt with in some other way (for example, by freezing). Care and thought must be given to the question at the time the specimen is obtained; it is often too late to change once some action has been taken. At the same time delay is seriously detrimental to good results. Special technical methods enable structures such as the chromatin components

of nuclei or mitotic figures, nerve fibres (Fig. III) or the Golgi apparatus (Fig. IV) to be clearly demonstrated.

One of the problems inherent in the use of fixatives is that they produce changes in the cellular components which, though rendering them more distinct, at the same time make them different from what they originally were. It is possible by using the freeze-drying method to avoid the use of fixatives and thus to obtain appearances which are a satisfactory check on the artefacts produced by various fixatives. This method may be used also for the preservation and demonstration of materials which would be dissolved out of the tissues by solutions used during the ordinary processing. This, however, requires special attention to detail, particularly in the early stages.

FIG. III. Photomicrograph of a section of a carcinoma of the breast showing a collection of tumour cells invading a nerve fascicle. The axons have been demonstrated by a silver impregnation technique. (x 360)

Bacteriology

Attention has been given here principally to the histological investigation of tissues as they are removed by the surgeon in the operating theatre. Bacteriological study of these tissues is also extremely important, particularly since the introduction of the antibiotics and the development of such complications as resistant strains, and the increasing knowledge of the organisms has been necessarily accompanied by an increasing number and complexity of techniques and cognizance must be taken of these. Not only must the material be kept apart from chemical agents which will kill the organisms (antiseptics, fixatives) but, especially when the bacteriologist is not immediately available, appropriate precautions must be taken with regard to temperature, humidity and in some cases the early provision of appropriate media.

The rapid recent development of knowledge of the viruses adds a further complication and, unless the surgeon and his staff deal with the tissue in an appropriate manner, opportunities for complete diagnosis and for investigation of obscure conditions will be irretrievably lost.

FIG. IV. Photomicrograph of a section of gastric mucous membrane removed at operation. The Golgi apparatus or net has been demonstrated by Da Fano cobalt nitrate technique. Careful attention to simple details gave this result. (x 360)

Biochemistry

Biochemical investigations are rapidly assuming an ever-increasing importance but most of these do not require special comment here as they are, for the most part, carried out on material obtained in the wards and are common to both medical and surgical cases.

Investigations are beginning to be made, however, on tissues and, since these must be

fresh, the material obtained in the operating theatre is the natural source. Such studies at the moment have been confined mainly to investigation of differences between the chemical constituents of tumour cells and the normal cells to which they are related. It is probable that studies of enzyme activity of cells of various organs, comparable with those that are being carried out in some animals, will before long also begin to play an important part in the study of some diseases.

Experimental Methods

The use of the experimental animal has been in vogue since the early surgeons of Alexandria — and possibly before this. It has been effective, however, as with surgery itself only in the last 100 years. Surgical procedures on animals have been used, especially in some countries, as a valuable means of enabling the prospective surgeon to obtain reasonable proficiency in his craft before practising on his patients. It has been of extreme value also in elucidating the nature of or the functional changes occurring in many conditions and apart from those of immediate interest to the surgeon the method has been continuously employed by the physiologist and the experimental pathologist. In recent times this experimental technique has been used advantageously by surgeons in developing new surgical procedures and the astonishing successes of thoracic surgery of the last two decades are in large measure due to the imaginative and judicious application of this technique. Without the use of these animal experiments it is probable that the surgical progress in these fields would have been delayed for several decades.

It is always important to remember that information obtained from one species of animal must be applied to another with care and with reservations. In some cases differences in the anatomical arrangement of structures and obvious physiological dissimilarities make a particular animal inappropriate where the information is intended to be applied directly to man. Even when such should not be the case, the application of such information must be made with care. When the precautions are observed the value of the method, as indicated by the successes of the last two decades just mentioned, needs no further statement.

MODERN METHODS

The various methods of investigation that have been discussed are those which are in action or available at the present time, but it is clear that another sudden enlargement of the scope of our activities is arriving. Methods of study, previously unknown, are now becoming commonplace in the laboratory and, just as simpler adjuncts in the last century gradually became incorporated in the armamentarium of the clinician, so it may be expected that the new methods of study will also be employed. Their number and complexity will mean that probably they will not be available for the physician or surgeon himself, even though he be an enthusiastic investigator, but it is certain that assistance will be available for the appropriate investigations.

Up to the present, attention has been directed to relatively gross changes in tissues and to the coarse structure of cells and their products. Chemical studies have also been on a similar primitive plane. Of course, this kind of information will always be required and, in many cases, for a considerable time to come, it will be adequate for the purpose of the clinician.

Studies of cells have now proceeded to the stage where not only small cell components like mitochondria are investigated but the constituent elements of these are now being distinguished and studied. This is being done on the physical side by the electron microscope, the spectrophotometer (ultra-violet or infra-red) and various forms of electrophoretic apparatus and on the chemical side by the study of the action of various enzymes in different cell components which can be separated from each other. Separation of these components can be carried out on disrupted cells by differential centrifugation which, to prevent dissolution of the material once the cell is broken, must be carried out in refrigerated apparatus.

This is a new field and demands techniques different from those used at present or modifications of them and so for the moment it is confined to the experimental laboratory. The application of any of these new procedures will require the same kind of re-orientation that was necessary when the light microscope and the test tube were first employed as adjuncts to simple clinical examination.

To take one — the electron microscope — as an example of these new devices, some of the differences become apparent. Compared with the magnifications of tens or hundreds of the ordinary microscope, this magnifies to thousands. In appropriate circumstances, extremely fine detail is demonstrable so that earlier fixation becomes essential; the conscientious investigator of the present era finds that he is usually too slow.

FIG. V. Electronmicrograph of a cell from the carotid body. In the protoplasm there are large particles—mitochondria, granules and vacuoles. The vacuoles are artefacts due to slight delay in fixation. Osmic acid fixation. (x 12,000)

With these very large magnifications much thinner sections are naturally necessary so that instead of the present sections of a thickness of 1/5000th of an inch, those of 1/1,000,000th of an inch or less are necessary. At the same time, necessarily only minute pieces of tissue can be fixed and examined so that, in general, only relatively homogeneous tissues can be studied. At the present time, the method is not applicable (as is the light microscope) for scanning a tissue or easily or rapidly comparing one part with another. It is applicable only to the elucidation of the structure of one particular part at a time.

Fixatives employed are limited since the most satisfactory are those which have a high atomic weight. Molecules of this kind stop the electron beam and thus result in a differential effect on the fluorescent screen or the photographic plate. The most satisfactory reagent at the moment is osmic acid and, apart from other factors, the cost of this reagent is a limiting factor of investigations which do not have a definite purpose.

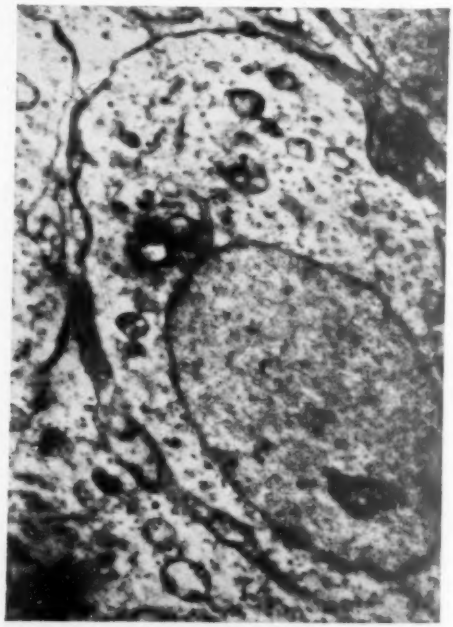


FIG. VI. Electronmicrograph of portion of a cell of the carotid body. The larger structures in the protoplasm are mitochondria. At still greater magnifications these are shown to have a characteristic structure of their own. Comparison of photographs of this kind with those shown in Figs. I and II gives some idea of the portent of this new technique. Osmic acid fixation. (x 12,000)

The material is embedded in a plastic rather than in paraffin or celloidin and cutting of the sections (which requires a special microtome) is an art which demands not only a specially skilled technician but one who has more than the average amount of patience and perseverance. Incidentally, the knife for cutting sections is made by the investigator himself from glass. No metal knife is able to produce sections of the thinness required.

Some of these details have been mentioned because clinicians are already beginning to look to this field and it is essential that it be appreciated that the difficulties, which incidentally are gradually and even rapidly being resolved, are formidable and require considerable laboratory study before the machine can be used in a routine manner. It is as yet a research tool but active co-operation between the surgeon and the interested investigator will hasten the day when it will be available for study of human tissues.

Some of the other types of apparatus mentioned can be applied more readily though, for some time, this will probably occur only in occasional cases and in those in which material is especially referred to the appropriate laboratory.

The difficulties in the application of the new types of equipment are not given to discourage those who may be interested. If we think of the state of affairs 100 years ago when the light microscope and the early equipment of the chemist and bacteriologist were beginning to become available we can from today's vantage point see that, at that time, failure to appreciate their potential value was understandable because of the great difficulties. With this recent history in mind, we should not now allow lack of vision to cause us to fail to take advantage to the greatest possible extent of what is available or neglect any attempt to promote and quicken this new wave of progress in which we are so fortunate as to be able to take part.

THE CLASSIFICATION OF ANO-RECTAL FISTULAE

By E. S. R. Hughes

Melbourne

In their paper published in 1934, Milligan and Morgan of St. Mark's Hospital, London, suggested a classification for anal fistulae which was both simple and practical, and one that was accepted widely. Their classification was as follows:

1. Subcutaneous and submucous fistulae.
2. Anal fistulae. These have their main tracks entering the anal canal below the ano-rectal ring and may be "low" or "high" level fistulae.
3. Ano-rectal fistulae. These possess a track extending above the level of the ano-rectal ring. Ano-rectal fistulae may communicate with the anal canal or with the rectum or may be incomplete.

A controversial feature of this classification has been the use of the term "ano-rectal" to designate the third group. A similar terminology has been adopted by many writers to describe specifically the type of fistula to which Milligan and Morgan refer. However, it has been used, and perhaps not unreasonably, to cover all the fistulae in the three groups. For example, in 1954, Coughlin published a paper headed "Ano-rectal fistula" which dealt with all types of fistulae; a year later, in the same surgical journal and under the same title, Bunney considered only those more complicated fistulae classified as "ano-rectal" by Milligan and Morgan (Coughlin, 1954; Bunney, 1955).

This lack of uniformity has caused confusion and has made it difficult for one to be clear at times as to which type of fistula is under discussion. In this investigation, a series of cases is analysed for the purpose of classification.

Material

A consecutive series of one hundred and one cases of anal fistula has been studied. These cases have been treated by the writer at the Royal Melbourne Hospital or in private practice and have all been subjected to operation. Seven other cases were examined, but are not included because operative treatment was not performed by the writer.

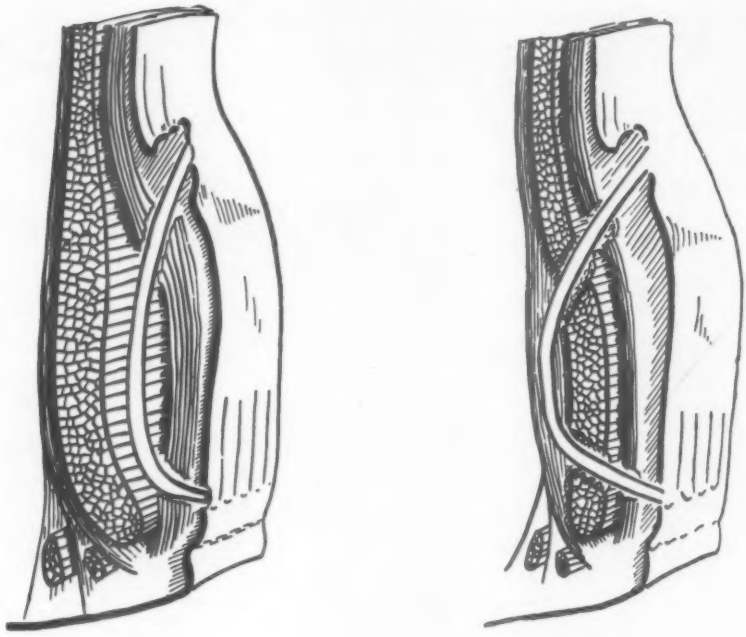
Findings

Submucous anal fistula (3 cases)

There were 3 cases of submucous anal fistula. In two others a peri-anal fistula was associated with a well-defined second fistulous track in the submucous space. In each there was an opening in the region of the anal valves and from here a track extended vertically upwards to open into the rectum a variable distance above the ano-rectal ring. By definition, the track lies in the submucosa, but in these cases the track passed deep to muscular tissue disposed both transversely and longitudinally in relation to the fistulous track; histologically, this was smooth muscle. This may be the muscularis mucosae muscle only which is well developed in this region, but it may include also part or whole of the internal sphincter muscle, although this is difficult to determine (Fig. I).

Peri-anal anal fistula (81 cases)

In 81 cases, the fistula was relatively superficial (Figs. II and III). From an external opening the fistulous track followed a straight or curved course into the anal canal. In 11 cases no internal opening was found and in three there was no external opening. In most cases the fistulous track passed through the internal sphincter muscle about one centimetre above the lower border; in some the track was so superficial as to be subcutaneous in the whole of its course, whilst in a few it seemed to enter the anal canal at a higher level than usual so that the amount of muscle tissue divided in effecting a cure was considerable. As the main fistulous track lay in the peri-anal space, this fistula has been referred to as a "peri-anal anal fistula." In 2 cases there was a localized extension into the neighbouring portion of the ischiorectal fossa, and in two there was a second fistulous track in the submucous space.



(a) (b)

FIG. I. Submucous anal fistula. The fistulous track may lie in the submucosa (a) or outside the internal sphincter muscle (b).

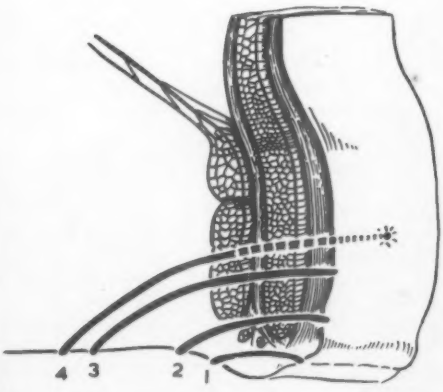


FIG. II. Peri-anal anal fistula.

1. Subcutaneous fistula (fistulette).
2. Low anal fistula.
3. High anal fistula.
4. Curved peri-anal fistula.

Ischiorectal anal fistula (24 cases)

In 24 cases the fistulous track was situated in the ischiorectal fossa. In three, the fistula commenced at an internal opening in the middle line anteriorly (anterior ischiorectal anal fistula), and in 20 cases in the middle line posteriorly (posterior ischiorectal anal fistula). In the remaining case, the internal opening was not found.

(a) Anterior ischiorectal anal fistula

From an internal opening in the middle line anteriorly in the anal canal, a fistulous track passed through the lowermost fibres of the internal sphincter muscle and then curved sharply to one side of the anal canal to enter the ischiorectal fossa, passing deep to the anterior branches of the inferior haemorrhoidal vessels (Fig. IV). In two of these cases the fistulous track communicated with an opening in the skin situated antero-lateral to the anus, whilst in the third, the external opening was postero-lateral. In this latter case the ischiorectal portion of the track

passed deep to the inferior haemorrhoidal vessels and then curved abruptly into the peri-anal space where it expanded into a large locule lined by granulation tissue. The fistulous track in these cases did not extend into the ischiorectal fossa as deep as the levator ani muscle, but nevertheless reached just above the level of the ano-rectal ring.

FIG. III. Typical peri-anal anal fistula. The fistulous track passes through the lower portion of the internal sphincter muscle.

(b) Posterior ischiorectal anal fistula

All of these possessed certain characteristic features similar to those described by Morgan (1949) (Figs. V and VI).

Internal opening. This was found in each case and was always situated in the anal canal in the middle line posteriorly, just below the ano-rectal ring. In one case there were two openings in the middle line posteriorly; one was in the typical position and the other about one centimetre below and associated with a secondary track in the peri-anal space.

Fistulous track. From the internal opening a short track, 1.5 centimetres to 2.0 centimetres in length, led directly backwards to join at right angles with the main fistulous track. This latter lay in the depths of the ischiorectal fossa; it coursed posteriorly, usually in very close relation to the levator ani muscle, curving around the posterior aspect of the anal canal to join with a similar track, if one was present, on the other side. This posterior connecting portion of the fistulous track lay deep to the coccygeal attachments of the external sphincter muscle and in very close relation to the puborectalis and pubococcygeus muscles. The short track leading from the internal orifice joined with this posterior communicating track.

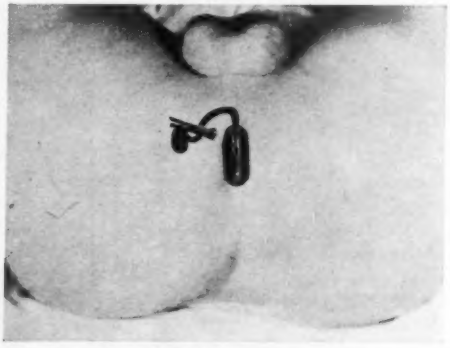


FIG. IV. Anterior ischiorectal anal fistula. The fistulous track is shown curving to the right and enters the ischiorectal fossa deep to the anterior branches of the inferior haemorrhoidal vessels.

In two cases the fistulous track was confined to the posterior aspect of the anal canal; from the internal opening the fistulous track extended into the deep post-anal space, but neither ischiorectal fossa was involved. In one of these there was no external opening, whilst in the other a deep post-anal abscess had been drained through an incision in the peri-anal skin, but this had closed completely. In 5 cases, the fistulous track involved the ischiorectal fossa on one side only, whilst in 13 both sides were affected and the fistulous track "horse-shoe" in shape. In two cases there was an extension into the supra-levator spaces through the thin iliococcygeus portion of the levator ani muscle. In one of these there was a typical internal opening into the anal canal, but no external opening; a track led through the levator ani muscle and caused a soft tissue swelling posteriorly in the region of the sacroiliac joint. In the other case, internal opening, fistulous (unilateral) track and external opening were present; at operation an extension through the levator ani muscle was found to end blindly in the supra-levator space. In neither of these two cases was there any communication with the rectum. In five cases secondary tracks were situated in the peri-anal space.

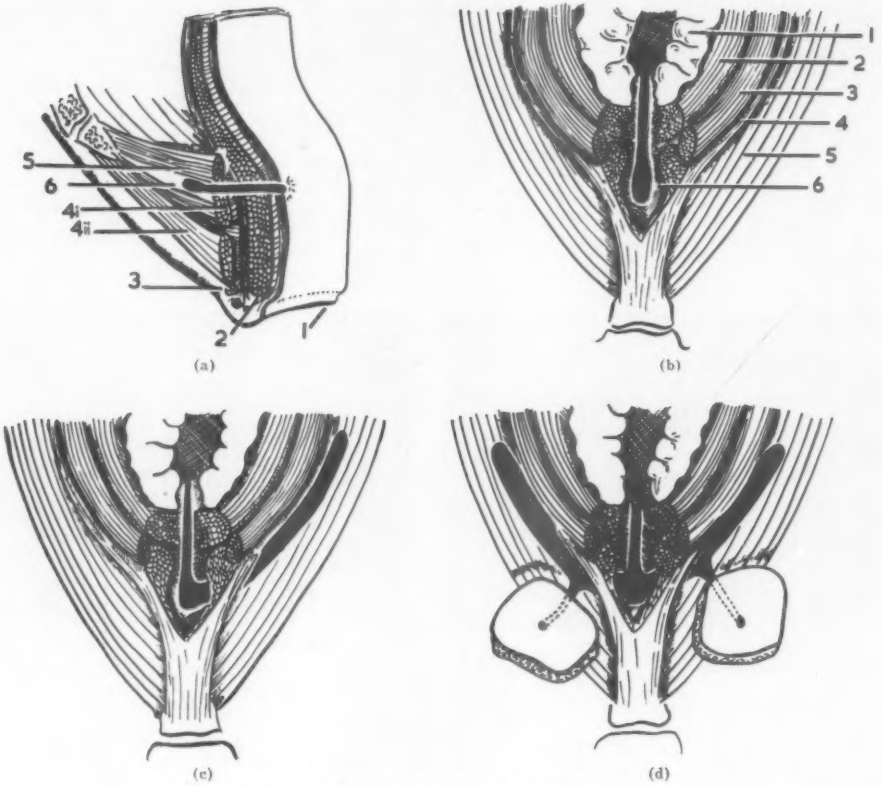


FIG. V. Posterior ischiorectal anal fistula.

1. Anal verge.
2. Internal sphincter muscle.
3. Subcutaneous external sphincter muscle.
4. Deep (i) and superficial (ii) external sphincter muscle.
5. Levator ani muscle.
6. Deep post-anal space.

(a) and (b) The fistulous track may pass from the internal opening to end in the deep post-anal space.
(c) The fistula usually extends into the ischiorectal fossa.
(d) Often, both ischiorectal fossae are involved with external openings on the peri-anal skin.

External opening. In 18 of the 20 cases there was, or had been, an external opening. This had no constant situation, but was placed usually some distance from the anal verge. In one case there were numerous openings on both sides of the anus, in three there were two external openings, but in the remainder there was only one actively discharging. From the external opening a track passed almost directly inwards to join the main fistulous track deep in the ischiorectal fossa. Usually, it was impossible to manipulate the probe through the external orifice and into the internal orifice because of the different directions taken by the component tracks. The probe appeared to pass directly upwards and on palpation the tip could be felt through the rectal wall above the level of the ano-rectal ring.

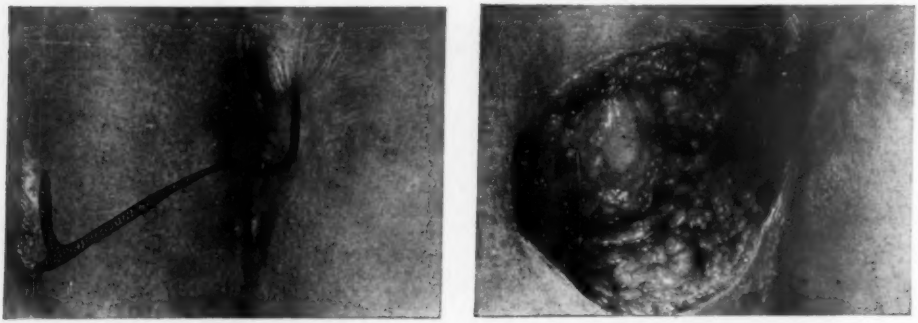
(c) Ischiorectal anal fistula without internal opening

In one case no internal opening was found and from subsequent experience it seemed likely that this case received inadequate surgery; it was the first case of the series and the only one which recurred.

Rectal fistula (3 cases)

In three cases there was direct communication with the rectum. In two cases the fistulous track was situated in the anterior segment and in the other it was posterior and may have been the sequel of a previous surgeon's attempt to cure an ischiorectal anal fistula. In the first two, the fistula closed spontaneously and the patients remained symptom-free, but in the third the discharge and discomfort persisted.

Thompson (1956) have also noted that a fistula may extend upwards between the internal and external sphincters along the main portion of the longitudinal muscle. However, as the internal and external openings are in positions similar to those found in the typical submucosal fistula, and as recognition is only possible at the time of incision of the overlying tissue, it seems best to regard this fistula as a deep variety of the submucous anal fistula.



(a) (b)

FIG. VI. Posterior ischiorectal anal fistula.

(a) The stippled portion of the track leads from the external opening to the ischiorectal portion of the fistulous track (black).

(b) The fistulous track laid open. The left side had been exposed at a previous operation although a persistent track remained.

DISCUSSION

The small number of patients with a submucous anal fistula conforms with the experience of others. The fistula is a sequel of a submucous abscess which is believed to be caused by an infection of the anal glands, although, if this is so, it is remarkable that these infections are not more common because it is unusual for these glands to pass deeper than the submucosa. The lower opening of the submucous fistula is felt as a tiny depression, whilst the upper forms a granulomatous projection as noted by Edwards (1918). In the three patients in this series the fistulous track lay deep to a layer of smooth muscle which was so thick that it seemed likely to be composed of internal sphincter muscle as well as muscularis mucosae muscle. Edwards (1918) observed that the fistulous track may lie outside the muscular coats and Miles (1939), aware of this classified the fistula as intermuscular. Naunton Morgan and

The peri-anal anal fistula is the sequel of a peri-anal abscess; the latter is by far the most common type of abscess and the corresponding fistula accounts for nearly 75 per cent. of anal fistulae. Milligan and Morgan (1934) referred to such fistulae as low level anal fistulae and believed that they entered the anal canal by passing between the lower border of the internal sphincter muscle and the subcutaneous portion of the external sphincter muscle; however, revised anatomical studies reveal that this fistula pierces the internal sphincter muscle as does the high level fistula (Goligher, Leacock and Brossy, 1955; Hughes, 1956). Miles (1939) termed these fistulae "subsphincteric," but his conception of the anatomy of the anal canal sphincters was different.

Milligan and Morgan (Milligan and Morgan, 1934; Morgan, 1949) referred to those fistulae in the ischiorectal fossa as "high level anal fistulae" and as "ano-rectal

fistulae," but the latter term is unsatisfactory because the rectum is very rarely involved and it is confusing on account of the tendency to call all fistulae in this region "ano-rectal." The terms anterior and posterior "horse-shoe" or "semi-horseshoe" fistulae are descriptive, but do not distinguish ischiorectal from peri-anal varieties. Miles (1939) described an "ischiorectal" and a "pararectal" fistula and stated that the latter may involve the ischio-rectal fossa and that when this was so, it may possess an internal opening in the middle line posteriorly.

In the 20 "posterior" types encountered in this series, there was an internal opening in the middle line posteriorly just below the ano-rectal ring. Morgan (1949) illustrates this type of fistula with an opening laterally situated, but no such variation was seen in this series. In two cases the fistulous track was confined to the deep post-anal space through which the two ischiorectal fossae communicated, but in the remaining cases the fistula extended into one or both ischiorectal fossae. In two of these posterior varieties there was an extension into the supra-levator or pararectal spaces, but it seems almost certain that this was secondary to the ischio-rectal infection rather than the reverse, because the features of the main fistulous track in these two cases were exactly the same as in the 18 cases without such extension. Morgan (1949) noted supra-levator extensions twice in 40 cases of ano-rectal fistulae. Since the anatomy of these fistulae is so closely linked with the ischiorectal fossa, it seems that the best term for them is "ischiorectal anal fistulae," a title also used by Wilson (1954). The "anterior" ischiorectal anal fistula is rare; in the 3 cases in this series the fistulous track reached above the level of the ano-rectal ring.

Because the internal opening of the posterior ischiorectal anal fistula is situated constantly in the middle line posteriorly (Tuttle, 1905; Lockhart-Mummery, 1934; Miles, 1939) it seems fair to assume that this is its site of origin. After the fistula has been laid open, the amount of muscular tissue remaining at the ano-rectal ring is so small that it appears certain that part, at least, of the levator ani muscle has been cut. This lends support to the view expressed by Courtney (1949) that abscess formation may originate between the layers of the levator ani muscle and later discharge into the ischiorectal fossa. However, the exact anatomical situation of the initiating abscess is of academic importance and for all practical purposes the main fistulous track occupies the deep post-anal space between the coccygeal attachments of the levator ani and external sphincter muscles.

If the fistulous track should enter the rectum above the anal sphincters, it is best termed a rectal fistula. This implies that all muscles composing the sphincter would have to be divided in order to lay open the fistulous track. There is still a tendency to adhere to the erroneous view expressed long ago by Allingham and others that an ischiorectal abscess often results in a rectal fistula (Allingham, 1882). From this study it seems that if an ischiorectal abscess does penetrate the levator ani muscle, it is exceptional for it to rupture into the rectum.

Type of Fistula	*No. of Cases*
Submucous	3
Peri-anal	81
Ischiorectal	24
Rectal	3
Total:	111

SUMMARY

1. A series of 111 cases of anal fistula has been studied.

2. There were 3 cases of submucous anal fistula. Each of these cases possessed a track which passed deep to smooth muscle. This muscle may be muscularis mucosae alone, but part or whole of the internal sphincter may be included.

3. The majority of anal fistulae were classified as peri-anal anal fistulae because they appeared to be the sequel of a peri-anal abscess. There were 81 cases; in 11 no internal opening could be found, whilst in 3 there was no external opening.

4. In 24 cases, the fistula appeared to involve primarily the ischiorectal fossa and, in most, to originate in the middle line

posteriorly, very close to the ano-rectal ring. The fistulous track lay in the deep post-anal space and usually involved one or both ischiorectal fossae. An external opening was absent in two patients. Secondary tracks may lie in the peri-anal space and, in two, secondary tracks passed through the iliococcygeus portion of the levator ani muscle.

5. In 3 cases the fistula coursed from an external opening in the skin to an internal opening in the rectum. The pathology of these was uncertain, but they did not appear to be a sequel of ischiorectal infection.

6. It is believed that the term "ano-rectal fistula" should not be applied to any one type of fistula, but should be used in the widest sense of the term to include all fistulae in the region. Classification should be revised to incorporate modern views on the anatomy of the region.

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TREATMENT OF ISCHIORECTAL ANAL FISTULA
(ANO-RECTAL FISTULA)

By E. S. R. Hughes

Melbourne

TO cure an ischiorectal anal fistula (ano-rectal fistula), it is an established principle that the fistulous track must be laid open. However, there are other features in the treatment of these fistulae about which opinion differs and which should be reviewed from time to time.

An ischiorectal anal fistula communicates with the anal canal just below the ano-rectal ring. The internal opening is close to the ano-rectal ring, so that the surgeon must be careful to avoid a too radical procedure because once this muscular ring is divided it is difficult to regain satisfactory function even with the most meticulous repair. On the other hand, unless the fistulous track be completely laid open, recurrence is inevitable. Goodsall expressed the view that it was better perhaps not to open the fistulous track between the posterior wound and the bowel, but Tuttle (1905) criticized this statement; " . . . this is the same old story which has so often been told in the treatment of fistula, an attempt to cure the condition by leaving the pathological cause untouched. If it were necessary to choose between leaving this or the lateral tracks unopened, by all means select the latter as complete healing would be much more likely to take place."

Most surgeons accept the need to divide this portion of the sphincter muscle in order to lay open the fistulous track, but many copy the practice of Goodsall, Miles, Lockhart-Mummery, Gabriel and others and perform a two-stage operation. At the first stage the fistulous track is laid open, but not that part leading through the anal sphincter muscle This is dealt with two or three weeks later when it is hoped that the fibrosis associated with the granulating wound will prevent retraction of the ends of the sphincter muscle, so minimising incontinence (Lockhart-Mummery, 1934; Miles, 1939; Gabriel, 1948). Other surgeons follow Tuttle's advice and complete the operation at one stage, claiming excellent functional results (Tuttle, 1905).

One of the most unfortunate aspects of the ischiorectal anal fistula (or ano-rectal fistula of Milligan and Morgan) is the long period of time desirable in hospital if the wound is allowed to heal in the orthodox way by granulation tissue. Between forty and sixty days must elapse before the granulation tissue has filled in the deeper parts of the wound sufficiently to permit relaxation of vigilance (Morgan, 1949). Attempts to shorten convalescence by primary suture were made over a century ago by Syme, later by Chassaignac, and subsequently by others, but it is a procedure which has never been popular with proctologists of experience because of the high recurrence rate with which it is associated.

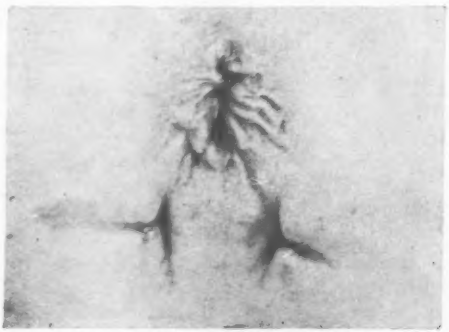

FIG. I. External openings of an ischiorectal anal fistula.

Present Series

In a series of 26 patients with ischiorectal anal fistula, 24 were subjected to surgery. Of the remaining two patients, one, a man of 57 years, had an ischiorectal abscess which required incision, leaving a fistula, but he deferred elective surgery on account of domestic difficulties, whilst the other, a man of 52 years, despite two operations for bilateral ischiorectal abscess, felt that the resulting fistula did not trouble him sufficiently to seek permanent relief. In the same period of time

that the 24 cases were treated surgically, 87 cases of anal fistula other than the ischiorectal variety were treated by operation.

There were 17 males and 7 females; the oldest patient was 65 years and the youngest 24 years. In 20 cases the internal opening was situated in the middle line posteriorly, in three it was in the middle line anteriorly, and in one it was not found.

ANATOMICAL FEATURES OF THE ISCHIORECTAL ANAL FISTULA

Posterior ischiorectal anal fistula (20 cases)

Each of these fistulae possessed certain features in common. The internal opening was situated in the middle line posteriorly, just below the ano-rectal muscular ring, and after the fistulous track had been laid open, only a very small amount of muscular sphincter remained intact. An external opening was not always present; in 2 of the 20 patients in this series it was absent, whilst in the remaining cases in which it was present, it was variably situated in relation to the anus, although usually towards the posterior aspect. The fistulous track commenced blindly, often above the triangular ligament, and passed posteriorly above the inferior haemorrhoidal vessels. It gradually became more superficial and curved posteriorly around the anal canal to enter the deep post-anal space situated between the coccygeal attachments of the levator ani muscle and of the superficial part of the external sphincter muscle. In this situation it joined with the track in the other ischiorectal fossa, if one was present; in this series, tracks on both sides of the anus were present in 13 cases, on one side only in five cases, whilst in the remaining two cases, the fistulous track was confined to the deep post-anal space. A short track from the internal opening passed directly posteriorly to join that part of the fistula lying in the deep post-anal space. A longer track passed from some part of the main fistulous track to the external opening. In two cases in this series, secondary tracks lead through the levator ani muscle and into the supra-levator spaces, but in neither was there direct involvement of the rectum. In 5 cases, secondary tracks were situated in the peri-anal space, causing confusion in diagnosis.

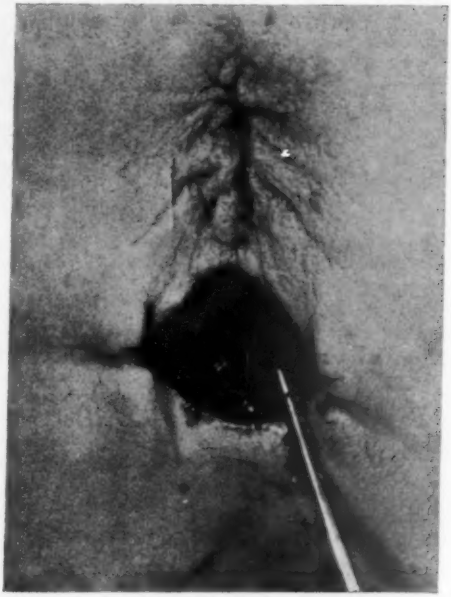

FIG. II. A superficial track joining these two openings has been unroofed and a probe has found a track leading into the right ischiorectal fossa.

Anterior ischiorectal anal fistula (3 cases)

In 3 cases a fistulous track involving the ischiorectal fossa opening into the anal canal in the middle line anteriorly; in two cases the internal opening was near the upper end of the anal canal, whilst in the third it was closer to the anal verge. The opening could not be palpated in any of these cases. An external opening was present in each case; in two, it was anterior to the transverse line through the anus, but in the third it was two centimetres behind this line. The main fistulous track involved the superficial part of the ischiorectal fossa, but passed deep to the anterior branches of the inferior haemorrhoidal vessels and curved anteriorly around the anal canal to enter it in the middle line anteriorly. In one case there was an extensive secondary track in the peri-anal space.

Ischiorectal anal fistula; internal opening not found (one case)

In the first patient of the series, a track in the left ischiorectal fossa communicated with an external opening, but the internal

opening was not found. That one was present is shown by the fact that it is the only one in the series which has recurred.

FIG. III. The track in the right ischiorectal fossa is laid open.

FIG IV. The floor of the wound in the ischiorectal fossa is very close to the rectum (the anal canal is retracted to the left).

ONE-STAGE OPERATION, WITH PRIMARY SKIN GRAFTING, FOR ISCHIORECTAL ANAL FISTULA

In the five days preceding the operation, the patient is given an intestinal sulphonamide (succinylsulphathiazole, 2½ grams, four times daily). An ordinary diet is permitted. The patient is admitted on the day before operation and an enema is given that evening. The perineum and both thighs are shaved, but the suprapubic region can be omitted.

FIG. V. A probe has found the track in the left ischiorectal fossa.

The operation is performed in the lithotomy position because it allows the transfer of the patient from operating table to bed with less chance of disturbing the dressings. General anaesthesia is preferred; following induction with thiopentone and relaxant, anaesthesia is maintained with nitrous oxide and oxygen. Laryngeal intubation is advisable because of the length of the operative procedure. In an operation of this nature extending over several hours, the blood loss may gradually reach an appreciable volume, and for this reason the anaesthetist should be prepared to give a blood transfusion if the need arises, although it was not necessary in any case in this series.

Posterior ischiorectal anal fistula

A probe is passed into the external opening and inserted as far as it will go. An incision is made anterior and posterior to this probe, so freeing it from the track in which it lies.

This incision will take the surgeon to the depth of the ischiorectal fossa, and in order to visualize the main part of the fistulous track which lies there, the skin edges are cut away freely (Figs. I and II). The probe is passed along the ischiorectal portion of the fistulous track as far anteriorly as it will go and it is freed by division of the overlying tissues; often this entails cutting the inferior haemorrhoidal neuro-vascular bundle. Overlying skin edges are cut back to improve exposure (Fig. III). Because of its proximity to this part of the fistulous track, great care must be taken to avoid perforating the rectum at this stage (Fig. IV).

FIG. VII. A probe has been passed along the track which leads through the anal sphincter muscle into the anal canal.

FIG. VI. The track has been laid open except for that part leading through the anal sphincter muscle.

The main ischiorectal fistulous track is traced posteriorly, around and in close relation to the anal canal (Fig. V). If there is a track in the other ischiorectal fossa, further probing behind the anal canal will disclose it. The tissue overlying the track is incised and again all the overhanging skin edges cut away freely to improve exposure (Fig. VI).

The track leading from the main fistulous track to the internal opening through the anal sphincter muscle is sought with a fine probe. Sometimes it is more easily found by inserting the probe from the internal opening rather than from the fistulous track, but it can be demonstrated in almost every case (Fig. VII). The anal sphincter muscle is divided down to the probe which is thereby freed (Fig. VIII); the whole extent of the fistulous track has now been exposed except for extensions through the levator ani muscle. These extensions should be sought by probing, and their presence recorded, but no further exposure is necessary.

FIG. VIII. A speculum has been placed into the anal canal and shows the amount of muscle to be divided to free the probe.

The open wound that has been created is ragged around the edge of the anus, but this can be corrected by suturing the fringe of peri-anal skin to the fascia covering the anal

sphincter muscle. Furthermore, the irregular edge of the divided anal sphincter muscle can be covered by suturing the skin of the anal canal to the same fascia (Fig. IX). The wound has now a regular surface and is well suited for skin grafting.

FIG IX. The wound is prepared for grafting by suturing the peri anal and anal canal skin to the fascia on the outer aspect of the sphincter muscle.

Sheets of free skin are cut as thinly as possible from the inner aspects of the thighs. These are transferred to the wound where they are sutured snugly into position and in such a way as to cover the whole wound (Fig. X). Fine instruments should be used for stitching the skin graft. The surface of the wound should be kept free of blood clot by repeated syringing. The graft is kept in place by covering it with *tulle gras*, over which is placed, layer upon layer, thin sheets of cotton wool soaked in saline. When the cavity has been filled firmly in this way, sutures are tied over the surface of the dressings to keep them in place. Further support is given by a combination of bandages and adhesive strapping (Fig. XI).

Anterior ischiorectal anal fistula

A probe is passed and freed in the same way as recommended for the posterior ischiorectal anal fistula. Skin is cut freely away in order to expose the deepest part of the track which is followed to the anterior aspect of the anus. The internal opening will be found only after the most painstaking search and the surgeon should be most reluctant to regard the operation as completed until this opening is found. The open wound is prepared and skin grafted in the same way described for the posterior variety.

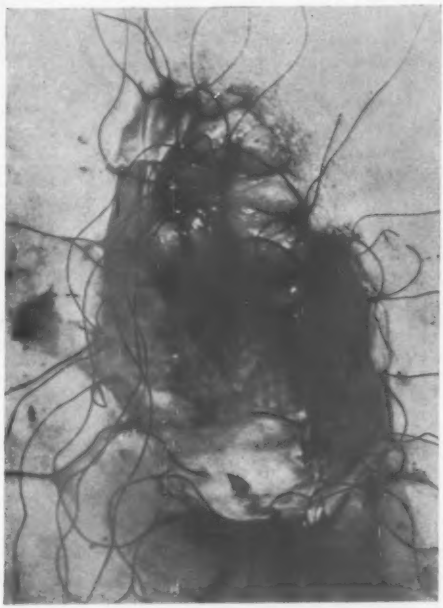

FIG. X. Sheets of thin skin are sutured into the wound and one to another.

FIG. XI. Adhesive strapping arranged to support the dressings over the grafted wound.

Post-operative treatment

At the conclusion of the operation the patient is lifted from the operating table on to his bed and arranged there so as to maintain the lithotomy position, although of much less exaggerated degree than at operation. The bowels should be kept confined until the first dressing on the fifth or sixth post-operative day. If flatulence becomes trouble-

some, the patient can be encouraged to expel flatus because the dressings are unlikely to be disturbed. There is surprisingly little difficulty with micturition in the male patients, but a self-retaining catheter is advisable for females. Chemotherapy or antibiotics in the post-operative period are not essential, but as their administration may improve the likelihood of success it has been the practice to prescribe penicillin and streptomycin for the first three or four post-operative days. The graft is inspected in the ward; no anaesthetic is required unless the patient be apprehensive. The sutures are cut and the cotton wool layers

FIG. XII. The wound on the seventh post-operative day, healed except for patches immediately behind the anus.

removed one by one, and finally the *tulle gras* is lifted off the surface of the wound (Fig. XII). In most cases there has been a satisfactory "take" of the graft. Any overlapping non-viable pieces of skin are cut away and the wound swabbed with mercurochrome (up to ten per cent.). The only dressing required after this is a small piece of cotton wool. The bowels are permited to open after the first dressing. The patient is allowed out of bed on the seventh day. For the next three or four days dressings should be done each day by the surgeon who is provided thereby with the opportunity of observing all parts of the wound. The patient returns home between the tenth and fourteenth days after operation. He is advised to have a bath after his bowel action and after cleaning the wound with clean cotton wool he should insert a small portion as an absorbent and as a protective. He should be reviewed by the surgeon in the first and second weeks after discharge from hospital (Hughes, 1954).

RESULTS OF THE ONE-STAGE OPERATION WITH PRIMARY SKIN GRAFTING

Mortality and morbidity

There have been no complications in this series. There has been no case of venous thrombosis despite the long period in the lithotomy position and the relative immobility in the post-operative period. One patient, a male of 65 years, had symptoms of bladder neck obstruction before the operation and it was decided not to graft his wound so that he could move more freely and get out of bed in the immediate post-operative period.

Success of the skin graft

In none was there less than a 50 per cent. surface "take" of the graft. In 20 cases the graft was successful (90-100 per cent.) and the wound healed at the end of the first week except for small areas between the sheets of skin. In three cases, between 50 and 85 per cent. of the graft was satisfactory, but part or whole of a sheet of skin had separated, either because of haematoma formation under the skin or because it had been displaced when the dressings were applied. Even that part of the graft in contact with fibrous floor of the fistula appears capable of succeeding. In one case, there was so much oozing from the wound that the graft was not applied until the second post-operative day.

Recurrence of the fistula

In the first case of this series the internal opening was not found and within a few weeks it was obvious that the wound possessed a discharging sinus in its centre. In all cases treated subsequently the internal opening was found and there has been no recurrence. It is appreciated that the true recurrence rate can be judged only after the elapse of ten or fifteen years because of the tendency of these

fistulae to remain dormant, but in 23 of these patients the wound has remained dry and the patient has had a feeling of comfort which has been missing in some cases for years.

Incontinence

In the first few days after the bowels resume activity, there is considerable weakness of the sphincter muscle, but usually within twelve days of the operation the sphincter is adequate in its function. Despite the fact that the amount of sphincter muscle remaining after laying open a posterior ischiorectal anal fistula is very small, no patient complained of incontinence when they returned for review three months after operation; 22 patients stated that the muscle seemed as strong to them as it did before the operation, whilst in two there was a tendency to leak if the motions became loose. In this one-stage operation combined with skin grafting, a large portion of the sphincter muscle is divided without any possibility of adherence of the ends of the divided muscle.

Prolapse of the rectum

There was no case of complete prolapse of the rectum after this operation, but in three cases there was a small but symptomless mucosal prolapse. The mucosal prolapse was situated at the site of the former internal opening.

Deformity

After laying open these long deep fistulae, a large cavity remains; if skin grafted this cavity looks forbidding at the time of the first dressings. However, within a few weeks the cavity becomes shallow, and no patient has complained of inconvenience caused by its presence.

DISCUSSION

The characteristic course of the ischiorectal anal fistula has been demonstrated by Naunton Morgan (1949) and his observations have been confirmed in this series. The complicated course of the fistulous track and its penetration of the anal sphincter muscle so close to the ano-rectal ring renders treatment an exacting task, but operation is facilitated by the basic similarity of the course pursued by the fistulous track.

The principle of laying open the fistulous track has always been accepted as a fundamental one and the experience obtained in this series of cases reaffirms this, although it may not be necessary to completely lay open the blind extremities. It is impracticable to lay open extensions through the levator ani muscle, but in any case this is apparently unnecessary because two cases in this series with supra-levator extensions were treated successfully by laying open the ischiorectal portion of the track only.

Division of two-thirds of the anal sphincter muscle has not caused incontinence as has been feared. It is remarkable how little muscle remains and yet proves adequate. Possibly the fibrosed fistulous track has interfered with the sphincteric action of the external sphincter muscle below the internal opening and subsequently has caused increased functional activity of the muscle above it (Miles, 1939).

The fistulous track of the ischiorectal anal fistula lies so close to the rectum and to the ano-rectal ring that safe excision of the fibrous track is impossible. Therefore, the fistulous track must be laid open and not excised; this excludes primary suture of the wound because if the track is laid open primary suture will reconstitute it. As there is no need for the fibrosis consequent upon healing by granulation tissue to preserve sphincteric function, it is unnecessary to allow these wounds to heal by granulation tissue. Simonetti (1954) advocates an operation which he terms "diathermic fistulotomy" and in which the tissue overlying the fistula is cut by diathermy, using a steel wire as an active electrode; but the complicated course of the track makes it difficult to pass a probe from external to internal opening unless it is laid open at operation. The results of one-stage excision and primary skin grafting have been very satisfactory and the time in hospital has been shortened to two weeks. The skin grafted cavity around the anus becomes less deep after a few weeks and its presence does not worry the patient.

CONCLUSIONS

The ischiorectal anal fistula possesses a complicated course, but the track can be found in most instances and laid open in one stage. The extensive wound can be covered successfully with a skin graft, applied at the initial operation. The functional results of this one-stage operation combined with a primary skin graft are excellent.

SUMMARY

1. A series of 24 patients with an ischiorectal anal fistula (ano-rectal fistula) were subjected to operation.
2. In 20, the fistula was classified as a posterior ischiorectal anal fistula because the internal opening was situated in the middle line posteriorly. The fistulous track ran in the ischiorectal fossa either on one or on both sides. An external opening was present in 18 and absent in two. Secondary tracks in the peri-anal and supra-levator spaces were sometimes present.
3. In three patients the fistula was classified as an anterior ischiorectal anal fistula because the internal opening was in the middle line anteriorly.
4. In one case no internal opening was found. It was the first case in the series.
5. In 22 of the 24 cases of this series the fistula was treated by a one-stage operation in which the whole track was laid open and the resulting wound covered by a primary skin graft. In one case the wound was too vascular and the graft deferred for two days whilst in the other case no graft was applied because of the desire to have the patient out of bed to void within a few hours of the operation.
6. Despite the long operation there has been no operative or post-operative mortality.
7. In 20 cases, 90 per cent. or more of the graft was successful and the wound almost healed within 7 to 10 days of the operation. In the remaining three cases part or whole of a sheet of skin failed either because of haematoma formation or because it had been displaced during the application of the dressings. In the least successful result there was approximately a 50 per cent. "take."
8. There was only one recurrence; this was in the first case of the series in which an internal opening was not discovered.
9. All patients were continent, although for a week or two after the operation there was a tendency for the sphincteric function to be inadequate. In 22 patients the sphincter muscle seemed as strong to the patient as it did before the operation. In the other two, there was some weakness when the motions became loose.
10. In three patients there was a small, symptomless partial mucosal prolapse.
11. The deformity produced by laying open and skin grafting this large fistula has not been a cause for complaint by any patient.

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RENAL CHANGES IN FATAL BURNS

A CLINICO-PATHOLOGICAL STUDY OF FOUR CASES

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THE study of the indirect visceral changes in severely burned patients has been less enthusiastic since the realisation that hepatic necrosis was mainly due to the absorption of tannic acid applied to the burned area. Changes in the renal morphology were noted by Gibson (1945) and clearly described by Goodpastor *et alii* (1946). Acute tubular necrosis has been recognised by Bull *et alii* (1950) and Oliver *et alii* (1951) as the pattern of renal damage likely to accompany oliguria and anuria from many different causes including severe burns.

The oliguria and anuria of the early post-burn phase are usually attributed to the loss of fluid and electrolytes into the burned area, and it is not generally realised that there may be actual damage to the renal parenchyma contributing to this oliguric phase.

It is the purpose of this paper to attempt a correlation of the clinical state, urinary output and renal histology in each of 4 patients who died of extensive severe burns.

Materials and Methods

The 4 patients studied were admitted to the Royal Melbourne Hospital between July and October, 1956. The first patient to be admitted had sustained extensive phosphorus burns and it was the anuria dominating the clinical picture which suggested a study of the structure of the kidney after death. The renal tubular changes found in this case were of such interest that liver and kidney aspirates were obtained in a further 3 patients admitted with extensive burns which proved fatal. These 4 patients died at different periods after injury and in this report their case histories are arranged numerically in order of length of survival.

Cores of liver and kidney tissue were obtained by percutaneous aspiration using a Franseen needle. This procedure was carried out within 30 minutes of death so that post-mortem autolytic changes were minimized. The tissues were fixed in 10 per cent. formal saline and paraffin sections were cut and stained with eosin and haematoxylin, and by the Wilder's silver impregnation method in order to examine the tubular basement membrane.

Autopsies were performed subsequently in Cases 2 and 3.

Case Histories

Details of the local care of the burns are not included in the following reports but in each case the limbs were dressed and the trunk and head exposed. In each patient fluids and electrolytes were administered intravenously according to standard principles. The urinary output charts are combined in Fig. I and the histology of the kidneys is summarized in the Table.

Case 1

An engineer, aged 49 years, was admitted fifty minutes after being severely burned by flaming oil from an exploding transformer. The estimated area of the burn wound was 65 per cent. of the total body surface. There were circumferential deep burns of both lower limbs excluding the feet, mixed deep and superficial burns of the whole back of the trunk, whole right upper limb, left hand and scalp, with mainly superficial burns of the face and neck. There was no evidence of respiratory tract involvement. The patient was conscious and rational.

The systolic blood pressure on admission was 160 mm. Hg., and pulse rate 84 per minute. Two litres of serum were infused within thirty minutes and 4 litres over the following five hours, during which time the blood pressure remained between 120 and 140 mm. Hg. and the pulse rate rose to 130 per minute. Seven hours after injury a coarse tremor with temporary loss of consciousness occurred, being described by the medical officer present as "epileptiform" and for which pethidine 75 mgms. was given intravenously. Half an hour later the respirations suddenly became shallow and the patient

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died, seven hours after injury. The mode of death, in the absence of hypotensive shock, suggests a cause of medullary failure other than anoxia.

Catheterization one hour after the injury yielded 14 cc. of heavily blood-stained urine. A further 10 cc. of blood-stained urine was obtained in the next two hours, 5 cc. in the fourth and fifth hours and for the last hour of life there was total anuria. The free serum haemoglobin concentration was estimated just prior to death as being 0.6 gms. per 100 cc.

Comment: Total anuria developed within six hours of injury despite a sustained blood pressure, but in the presence of haemolysis with haemoglobinaemia and haemoglobinuria. Early changes of renal tubular necrosis were present (Fig. II) and the liver cells showed slight vacuolization of their cytoplasm.

Case 2

A chemical engineer, aged 51 years, was admitted forty-five minutes after he had fallen into a tank containing metallic phosphorus stored under water. The adherent phosphorus had spontaneously ignited when the patient was removed from the tank. He had been rushed under a shower and a first-aid attendant had applied 1 per cent. copper sulphate to the burned areas. On admission, the patient was conscious and co-operative.

The estimated area of the burn was 60 per cent. of the body surface. There were deep circumferential burns of the legs excluding the feet, deep burns of the whole of the right and upper part of the left arm. Deep burns also involved the scalp, face, neck, front of chest and abdomen, genitalia and buttocks. There were superficial scattered burned areas on the back. There was also evidence of superficial damage to the oral cavity and upper respiratory tract and his breath had a peculiar garlic odour.

The systolic blood pressure on admission was 160 mm. Hg. and pulse 90 per minute. Intravenous therapy was commenced immediately. Two and a half litres of blood and serum and 2½ litres of fluids containing electrolytes and glucose were infused within the first eight hours. Over the next sixteen hours the same volume of blood, serum and electrolyte fluids were infused and thereafter continued at half this rate until death occurred forty-eight hours after injury.

During the first thirty-six hours the blood pressure remained between 110 and 130 mm. Hg. and the pulse about 100 per minute. There was no increase in venous pressure, no evidence of pulmonary congestion. Thirty-six hours after admission the patient became drowsy and irrational, the skin of the feet was cyanotic and there was poor capillary return on pressure. The blood pressure at this stage was 100 mm. Hg. and the pulse 110 per minute. The patient became deeply comatose forty-six hours after admission with rapid shallow respirations and he died soon after.

Catheterization one hour after injury yielded 50 cc. of heavily blood-stained urine. In the next three hours the hourly urinary output was only 10 cc., and after six hours this fell to 1 or 2 cc. hourly. For the last twenty-four hours of life anuria was complete.

Autopsy revealed swollen kidneys with medullary congestion. The liver was macroscopically normal and there was a fine bilateral emphysema and anthracosis of the lungs obviously of some standing.

Comment: Early haemoglobinuria and severe oliguria became total anuria within twenty-four hours despite a sustained blood pressure. Peripheral failure became evident just prior to death in anuria at forty-eight hours. The kidney showed acute tubular necrosis (Figs. III and VI), with tubular basement membrane disruption (Fig. VII). No phosphorus was detected in the kidney at a subsequent chemical analysis. The liver cell changes were of a minor degree (Fig. VIII) and quite unlike the gross fatty infiltration associated with phosphorus poisoning. This evidence suggests that phosphorus absorption played little or no part in the damage to the kidney. The mode of death in this case may have been biochemical, the combination of renal and pulmonary pathology preventing a normal acid-base balance.

Case 3

An engineer, aged 35 years, was admitted fifty minutes after having been severely burned by flaming oil from an exploding transformer. It was estimated that the burn area covered 70 per cent. of the body surface. There were circumferential deep burns of all limbs, chest, buttocks and part of the back. The scalp, the whole of the face, and the mucosae of the lips, anterior oral and nasal cavities were completely charred. The patient was conscious and not complaining of pain but early signs of respiratory distress were present so that half an hour after admission to hospital a tracheotomy was performed, with immediate relief.

The systolic blood pressure on admission was 150 mm. Hg. and pulse rate 120 per minute. Resuscitation was begun immediately and within eight hours 1.5 litres of blood, one litre of serum and 2 litres of electrolytes and glucose fluid had been infused. During the following sixteen hours the same volume of blood, serum and electrolytes was given and continued at half this rate until 48 hours after admission.

The blood pressure in the first twenty-four hours varied between 120 and 150 mm. Hg. and the pulse rate was 106 per minute. There was no change in his clinical state until the third day, the patient remaining alert and rational. The haemoglobin had fallen from 160 per cent. on the 1st day to 110 per cent. The blood pressure had risen to 170 mm. Hg. and the pulse rate was constant at 100 per minute. Intravenous therapy was reduced as intragastric tube feeding was begun.

The patient became drowsy on the fifth day, with the blood pressure at 120 mm. Hg. and haemoglobin at 96 per cent. There were widespread rhonchi in the chest. The pulse rate was approximately 140 per minute, and frequent extrasystoles were present.

On the sixth day the patient appeared exhausted and was difficult to rouse. The respirations were shallow and rapid, becoming irregular and gasping until he died.

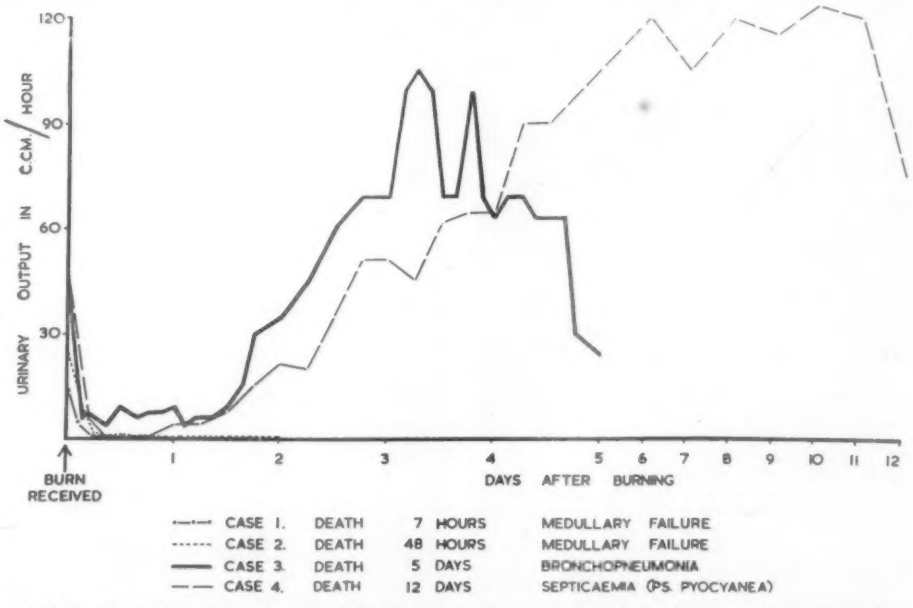

FIG. I. The urinary output charts of 4 fatally burned patients are superimposed to show the pattern of early oliguria and anuria. Subsequent diuresis occurred in the 2 patients surviving longest. The renal histology can be correlated with these charts.

Catheterization ninety minutes after injury yielded 90 cc. of heavily blood-stained urine. The output for the third hour was 5 cc. and 7 cc. for the fourth. Over the next 12 hours the hourly urinary output remained between 3 and 10 cc. but the urine became macroscopically clear of blood and the specific gravity varied between 1010 and 1012. The total urinary output for the first day was 325 cc., including the 90 cc. present on admission. During the second day the hourly urinary output rose from 3 cc. to 35 cc. and the total daily output was 455 cc.

The hourly flow on the third day rose to 70 cc. and on the fourth to 105 cc. with daily output of 1335 cc. of clear urine with specific gravity 1010. During the fifth and sixth days the urinary output began to decrease with specific gravity 1010 to 1012.

Autopsy revealed a staphylococcal bronchopneumonia and several small splenic infarcts of recent origin.

Comment: Again oliguria with haemoglobinuria were seen soon after the burns were received and persisted despite early resuscitation. The diuretic phase began on the fourth day. This sequence corresponded to a histological appearance of tubular necrosis and early tubular regeneration in the kidney (Fig. VI). It is probable that the severe staphylococcal infection accentuated the tubular degeneration but clearly could not account for the regenerative changes which must have been pre-existent. The splenic infarcts are evidence in favour of an ischaemic episode affecting the viscera.

Case 4

A carrier, aged 25 years, was admitted three hours after his motor truck had crashed and ignited. He had been concussed and severely burned. The estimated extent of his burn was 40 per cent. of the body surface. There were circumferential deep burns of both lower limbs, patchy on the left leg and excluding the feet, with deep burns also of the buttocks, back of the right forearm, both hands and face, with superficial areas over the neck, arms and perineum.

The systolic blood pressure on admission was 140 mm. Hg. and the pulse rate 124 per minute. One and a half litres of blood, 1½ litres of serum and 2 litres of electrolyte fluids were infused within eight hours, and repeated during the next sixteen hours. Blood, serum and electrolytes were continued at half this rate for a further twenty-four hours.

THE HISTOLOGICAL FINDINGS IN THE KIDNEYS OF FOUR FATALLY BURNED PATIENTS.

Case and survival time	*Glomeruli*	*Convoluted tubules*			*Comment*
		Epithelium	*Lumen*	*Basement membrane*	
Case 1 seven hours	Patchy dilatation and congestion. Exudate in capsular space.	Areas of swelling and granularity. Occasional frank necrosis.	Numerous pigment, hyaline and granular casts and red cells.	Minimal patchy disruption.	Early acute tubular necrosis.
Case 2 forty-eight hours	Slight dilatation and congestion. Exudate in capsular space.	Extensive patchy necrosis and desquamation.	Numerous pigment, hyaline and granular casts.	Extensive patchy disruption.	Established acute tubular necrosis.
Case 3 five days	Minimal congestion and exudate.	Extensive patchy necrosis. Low regenerating epithelium.	Dilated in regenerating areas. Few casts.	Patchy disruption.	Acute tubular necrosis. Early tubular regeneration.
Case 4 twelve days	Normal.	Areas of regenerating and mature tubular epithelium.	Regenerating tubules dilated. Few casts.	Intact.	Tubular regeneration

From the beginning the patient was conscious and alert, the pulse varying between 85 and 115 per minute. On the third day intravenous therapy was replaced by an intra-gastric drip through which 2 litres of high caloric fluid were given daily in addition to oral food and fluids.

The clinical state of the patient was excellent until the ninth day. At this time he had *Ps. pyocyanea* infection of the burned areas on the thighs. On the eleventh day he became stuporose, with the blood pressure at 130 mm. Hg., pulse 120 per minute and Hb. 98 per cent. There were signs of bilateral bronchopneumonia. Next day there was neck stiffness, the respirations were rapid, shallow and gasping, and he died in coma twelve days after injury. Blood culture taken in the last twenty-four hours of life grew *Ps. pyocyanea* insensitive to penicillin, streptomycin and the broad spectrum antibiotics.

Catheterization almost 4 hours after injury returned 240 cc. of heavily blood-stained urine. During the next three hours only 42 cc. of blood-stained urine were obtained and a period of complete anuria followed for ten hours. The flow recommenced with 3 to 5 cc. of only slightly blood-stained urine hourly, and steadily improved during the second day until 20 cc. hourly were passed with a daily total of 360 cc. The hourly output increased to 50 cc. during the third day, 65 cc. during the fourth day, 90 cc. during the fifth and 100 to 120 cc. from the sixth day until just before death. The average daily output over these last five days was 2800 cc. and the specific gravity between 1010 and 1012.

Comment: Early oliguric and anuric phases with haemoglobinuria and similar time relationships to the previous 3 cases are noted. The diuretic phase began on the third day and was maintained until *Ps. pyocyanea* septicaemia caused a rapid deterioration in his condition on the eleventh day. The renal histology showed areas of tubular regeneration (Fig. VII). These changes were so advanced as to be clearly unrelated to the terminal infection.

In this series of 4 severely burned patients early oliguria and anuria occurred in the absence of a hypotensive phase. Severe haemoglobinuria was a constant feature in the early stage.

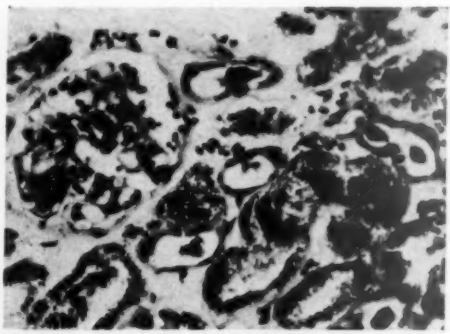

FIG. II. Case 1: Early post-mortem renal aspirate from patient dying seven hours after receipt of severe burns. There is a granular degeneration of the tubular epithelium, and pigment casts are present in the tubular lumina. Haematoxylin and eosin. (x 300)

Histological examination of tissue fragments obtained by needle aspirations immediately after death showed the presence of kidney damage, mainly in the tubular epithelium, patchy in distribution, and associated with disruption of the tubular basement membrane in the two cases with frank tubular necrosis.

Although the small number of cases precludes any final conclusions regarding the nature of the burns, the kidney changes and their time relations, an opportunity to assess the probable progress of these changes was afforded by the deaths of these patients having occurred at increasing intervals after burning. Patchy tubular damage was present within seven hours (Fig. II) and frank necrosis at forty-eight hours (Fig. III). This tubular necrosis was associated with glomerular stasis and protein exudate, heavy deposition of casts, including pigment casts in the tubules and medullary congestion and oedema. Tubular regeneration from scattered surviving epithelium was in evidence on the fifth day (Fig. IV) and was well advanced at twelve days (Fig. V). This phase of tubular regeneration coincided clinically with a profuse and prolonged diuresis.

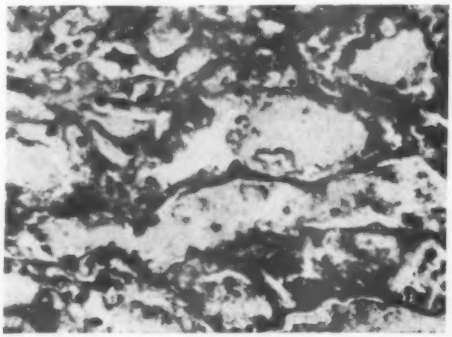

FIG. III. Case 2: Renal aspirate from patient dying two days after receipt of severe burns, showing necrosis and desquamation of tubular epithelium and casts in lumen. Haematoxylin and eosin. (x 300)

Slight liver cell damage was seen in the first case as early as seven hours after injury. This consisted of some vacuolation of polygonal cell cytoplasm and loss of cell outline. These changes were less marked in the subsequent cases, and some regeneration of liver cells was present in Cases 3 and 4.

DISCUSSION

The two factors known to contribute frequently to renal tubular damage and present in all these 4 cases, are massive trauma and haemolysis. The role of trauma is mainly in the production of reflex renal vasoconstriction which was shown experimentally by Keele and Slome (1945) to reduce renal blood flow to one-half normal within one minute. Cineradiography of the intrarenal circulation by almost immediate diminution of renal blood Trueta and co-workers (1947) confirmed this flow on intravenous administration of adrenalin, faradic stimulation of the sympathetic plexus surrounding the renal artery or stimulation of the major peripheral sensory nerves. In these patients the absence of hypotension in the "oligaemic phase" is attributed in part to resuscitation and in part to this visceral vasospasm.

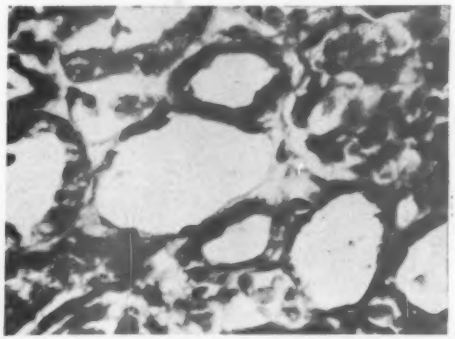

FIG. IV. Case 3: Renal aspirate from patient dying five days after receipt of burns. There has been desquamation of necrotic tubular cells and flattened regenerating cells are appearing. Haematoxylin and eosin. (x 500)

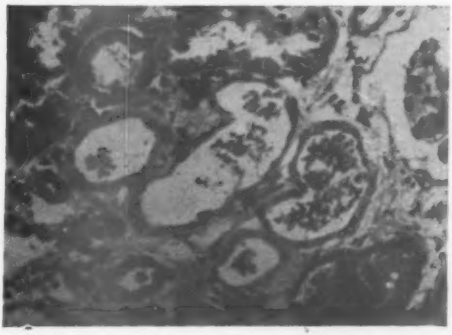

FIG. V. Case 4: Post-mortem renal aspirate taken twelve days after receipt of burns. There are regenerating tubules lined by flattened epithelial cells with irregularly spaced nuclei. Mature tubules adjacent. Slight increase in interstitial tissue and lymphocytes. Haematoxylin and eosin. (x 300)

It is postulated that an extensive deep burn produces an intense immediate, although transient, stimulation of the sensory nerves in the burnt area before necrosis occurs, thereby

producing an instantaneous general reflex response as distinct from the slower trauma of an extensive surgical operation or of the "crush injury". The early onset of oliguria in these burned patients is therefore to be expected, and, although the immediate pain stimulus soon subsides, there is the possibility of the reduced renal blood flow being rendered permanent by a prolonged oligaemic shock phase.

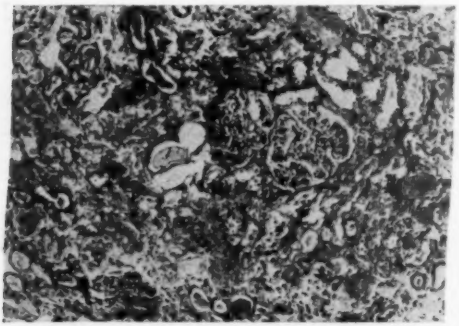

FIG. VI. Case 2: Renal aspirate showing patchy nature of tubular necrosis, desquamation of epithelium and casts. Haematoxylin and eosin. (x 150)

The role of haemolysis in the production of renal tubular damage is not precisely known. Free circulating haemoglobin is not in itself toxic to the tubular epithelium (De Navasquez, 1940), but there is abundant experimental evidence to show that the combination of free haemoglobinaemia with some renal ischaemia, whether from shock (Yuille *et allii*, 1945) or renal artery occlusion (Badenoch and Darmady, 1948), greatly increases the incidence and degree of tubular damage. In surgical practice there is further evidence of this synergism in the increased risk of anuria after major surgery in patients with haemolysis.

The scanty volume and heavy blood-staining of the urine found in the bladders of these patients within a short time of burning reflect the very early occurrence of the changes in the blood and intrarenal circulation. The presence of pigment casts and frank blood in the tubules of Case 1 within seven hours of injury confirms this change and the histology indicates definite early tubular cell damage (Fig. II). This man became completely anuric one hour before death and it is possible that this coincided with the onset of the tubular epithelial degeneration. The precise mechanism of this anuria is not clear, but it is probable that failure of glomerular filtration combined with free diffusion of filtrate back through the damaged cell membranes of the tubular lining is encouraged by some distal tubular obstruction from swollen disquamating cells and pigment casts.

The glomeruli at seven hours showed some capillary stasis and protein exudate consistent with a severe anoxic phase. The persistence of a diminished intrarenal blood flow and glomerular filtration rate despite early relief from the pain stimulus and adequate circulatory resuscitation is largely attributable to the oligaemic phase and coincident haemoglobinaemia and haemoglobinuria.

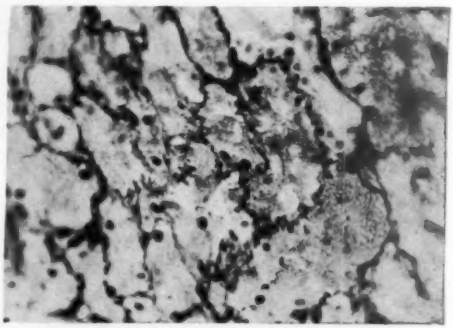

FIG. VII. Case 2: Renal aspirate showing disruption of tubular basement membrane. Wilder's silver impregnation technique. (x 300)

The presence of definite tubular necrosis as early as seven hours after injury (Fig. II) is not consistent with the findings of Dible (1953) that the earliest histoligical changes were found after thirty to forty hours' anuria. There are two possible explanations of this difference. In the cases studied by Dible autopsy material was used and it is probable that post-mortem autolysis had overshadowed these early changes of tubular necrosis. Also Dible's series of 40 cases included only 2 burned patients — it consisted mainly of patients with incompatible transfusions, crushing injuries and other haemolysing agencies of a less intense and instantaneous nature than the sudden severe injury in burns which may account for the earlier onset of tubular necrosis.

From the patchy distribution of the lesions (Fig. VI) and the disruption of the basement membrane in the areas of greater tubular damage (Fig. VII), the pattern appears to be one of multiple infarction at different levels of the nephron rather than a diffuse cellular necrosis of the whole tubular lining. The significance of the patchy lesions with the disruption of basement membrane has been shown by Oliver (1953) using microdissection of tubules to lie in the ischaemic origin of the tubular lesion as opposed to a toxic factor acting diffusely on the epithelial cells of the tubules alone.

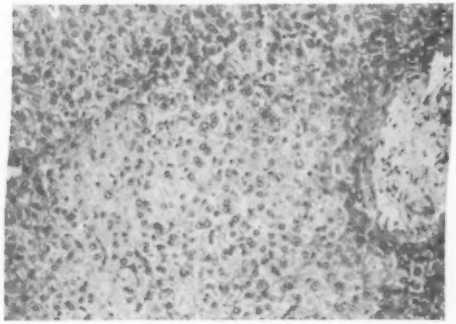

FIG. VIII. Case 2: Liver aspirate showing only slight vacuolation of liver cells, in contrast to severe renal changes in Figs. III and VI. Haematoxylin and eosin. (x 150)

Epithelial regeneration from surviving cells was seen to be present as early as the fifth day, reconstituting the tubular lining with flattened syncitial cells with irregular nuclei, occasional mitoses and a larger tubular lumen with some protein exudate but no pigment casts (Fig. IV).

The morphological immaturity of these newly reconstituted tubular linings has been demonstrated by the failure to stain mitachondria and by the absence of such normal cytoplasmic enzymes as lipase and alkaline phosphatase (Oliver, 1951). Functional immaturity of the tubular epithelium was shown by the persistence of a low urinary specific gravity irrespective of the daily volume passed.

In the burned patient the diuresis coincides with the resorption of vast amounts of water, protein and electrolytes from the burned area as the damaged capillary walls return to normal permeability. This may account for the earlier diuretic phase in these patients than in those with "crush syndrome" where it is more usual after four or five days. The diuresis is attributable on the renal morphology to the patchy nature of the damage and the earlier recovery of the glomerulus, which is not so severely damaged as the tubules, so that filtrate is delivered into the tubular lumen before this epithelial lining has fully recovered its integrity, let alone its ability to resorb water. Hence, once the oedema of the wound area has been resorbed, dehydration may occur in this phase, with electrolyte depletion directly attributable to this pattern of renal damage.

The possibility of parenchymal renal damage should be borne in mind during the resuscitation of severely burned patients. While it is very likely that this tubular damage occurs only in the severely burned, at the same time it is in this group of patients that large volumes of fluid must be infused rapidly to combat the shock phase. It is suggested that three points bear consideration. First the evidence of blood destruction together with the need to minimise visceral anoxia further support the current use of whole blood in the resuscitation of deep burns. Second, considering the enormous volume of fluid infused in the first 24 hours after a severe burn at the same time as renal parenchymal necrosis is developing, the need for very strict control of any subsequent fluid therapy is obvious. For if infusion is continued after forty-eight hours the risk of over-loading the circulation becomes very real. Finally, in the diuretic phase the regenerated tubular lining contributes to the danger of major fluid and electrolyte depletions by its inadequate capacity for resorbing these elements. The morphological findings in these cases stress the necessity for further studies of renal function in severe cases of burns.

SUMMARY

The case histories are reported of 4 patients with extensive burns, all showing the common features of early oliguria or anuria with severe haemoglobinuria in the absence of a hypotensive phase as estimated by the systolic blood-pressure.

The renal histology was studied in aspirates taken immediately after death and revealed varying phases of acute tubular necrosis. As-

the patients died seven hours, forty-eight hours, five days and twelve days after injury, it was possible to observe both the early and the late changes present in the tubular epithelium. The necrosis was most pronounced in the forty-eight hours' specimen corresponding clinically to total anuria. At five days tubular regeneration had commenced, coinciding clinically with the early diuretic phase.

The production of these renal changes is discussed and it is suggested that renal vasospasm, haemoglobinaemia and oligaemia are the principal contributing factors. An appreciation of the renal changes is of value in the planning of treatment.

ACKNOWLEDGEMENTS

We wish to thank Mr. B. K. Rank and Dr. Ian Wood for their advice in the preparation of this report. The chemical analysis for phosphorus in the kidney of Case 2 was kindly performed by Dr. N. McCallum of the Department of Pathology, University of Melbourne.

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CORTICOID REPLACEMENT AFTER ADRENALECTOMY WITH SPECIAL REFERENCE TO THE USE OF FLUOROHYDROCORTISONE

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IN assessing the relative merits of adrenalectomy and hypophysectomy for disseminated cancer of the breast it is necessary to consider the advantages and disadvantages of each procedure.

Adrenalectomy is as a rule combined with oophorectomy and the whole procedure is normally performed in two operations; it is, however, relatively simple and safe, and is within the compass of any competent general surgeon. Hypophysectomy is completed in one operation, but is a more hazardous procedure and should be performed only by a trained neurosurgeon. From the point of view of simplicity and safety of the operation, therefore, adrenalectomy has a decided advantage.

On the other hand it is claimed that hypophysectomy is likely to be more effective in controlling the disease, and that the hypophysectomised patient can be maintained after operation more easily than the adrenalectomised patient.

The first of these claims is suggested by theoretical considerations, because there are pituitary hormones which act directly on the breast in addition to those which act via the adrenals and gonads, but whether it is true in practice remains to be seen.

The second claim is undoubtedly true if cortisone or hydrocortisone is the only hormone available. These steroids have a predominantly glucocorticoid action and have relatively little effect on electrolyte metabolism; if used alone, therefore, they may fail to maintain a proper balance in the adrenalectomised patient despite a full ration of salt. There is, of course, no necessity for any such limitation, though many surgeons have imposed it on themselves, and the situation may be much improved by administering cortisone in combination either with another steroid having a more pronounced mineralocorticoid action, or with liquorice (glycyrrhetinic acid), which has been shown to have a deoxycortone-like action in normal subjects, and also in patients with Addison's disease who are receiving cortisone (Borst, Holt, De Vries and Molhuysen, 1953). Alternatively, if a steroid having appropriately balanced mineralocorticoid and glucocorticoid effects could be found it could be used alone.

Hart (1956) has used deoxycortone in combination with cortisone in adrenalectomised patients showing evidence of sodium depletion, and had reported briefly on the use of 9α-fluorohydrocortisone, alone and in combination with cortisone.

We have used 9α-fluorohydrocortisone in two patients subjected to adrenalectomy for disseminated cancer of the breast. One patient, with a malignant pleural effusion, obtained no benefit from one operation and died a few weeks later. The other patient has now been maintained for more than 12 months, initially on 9α-fluorohydrocortisone and subsequently on this substance and cortisone in combination, and has been studied in some detail.

Case Report

Mrs. V.T., 46, had a radical mastectomy performed for a stage II carcinoma of the left breast in April, 1954. This was followed by post-operative deep X-ray therapy. In November, 1954, she complained of pain in the back and right leg, and radiological examination revealed metastases in the acetabulum on the right side and in the head of the right femur. She was treated in another clinic with deep X-ray therapy and stilboestrol*. The pain became worse and between February and June, 1955, she was given further deep X-ray therapy and a course of testosterone. When seen by one of us in October, 1955, she complained of severe pain and was unable to walk unaided. She was emaciated, and radiological examination revealed widespread bony deposits in the ribs, spine, pelvis and upper femora. Surgical oophorectomy was performed and it was decided, after

* In our view oestrogens should never be administered to a woman of this age with metastatic breast cancer.

consultation with Sir Stanford Cade, to follow this with bilateral adrenalectomy. Accordingly, the right adrenal gland was removed on 18th November, 1955, and the left adrenal 10 days later. Following operation the patient was given 9α-fluorohydrocortisone acetate (referred to hereafter briefly as fluorohydrocortisone) by mouth, at first alone and later in combination with cortisone.

METABOLIC STUDY

Observations were made of the patient's weight, blood pressure, urinary output, urinary sodium and potassium, serum sodium and potassium and fasting blood sugar, at first daily and later as seemed necessary. These data, together with the post-operative replacement therapy, are summarised in Table 1.

It will be seen that after the right adrenalectomy the urinary Na^+/K^+ ratio, which is usually between 1 and 3, fell sharply, indicating retention of sodium at the expense of potassium. It was probably due partly to the administration of fluorohydrocortisone and partly to production of aldosterone by the opposite adrenal in consequence of the operative trauma (Llaurado, 1955; Llaurado, Neher and Wettstein, 1956; Llaurado and Woodruff, 1957).

Following removal of the left adrenal the blood pressure fell to 75 mm. of mercury systolic. Noradrenalin was administered by a slow intravenous drip for 2 hours, at the end of which time the blood pressure was 105/70 mm. of mercury, and thereafter the patient's condition caused little anxiety. Fluorohydrocortisone was given in large dosage (5 mg. the day before operation and on the day of the operation, reduced thereafter to 4, 3 and 2 mg. daily on succeeding days as shown in the table), and this caused intense sodium retention with corresponding excretion of potassium, indicated by a sharp fall in the urinary Na^+/K^+ ratio and a rise in the serum Na^+ to 160 mEq/l. The serum Na^+ returned to normal 2 days later but the urinary changes persisted much longer. The day after operation (the thirteenth day of the metabolic study) there was a slight increase in the fasting blood sugar, which was presumably also due to the high dosage of fluorohydrocortisone.

On the twentieth day of the metabolic study the patient was free of pain and was able to walk unaided. On the twenty-fourth day a condition resembling diabetes insipidus appeared, characterised by intense thirst and high fluid intake and output. The urine still showed evidence of marked sodium retention and potassium excretion but it is noteworthy that there was neither oedema nor gain in weight. It was decided to maintain the dose of fluorohydrocortisone at 2.0 mg. daily but to increase the intake of potassium by administering potassium chloride in a dosage of 3 g. daily. The urinary electrolyte levels became more normal but the serum K^+ fell to 3.0 mEq/l. The daily dose of fluorohydrocortisone was therefore reduced on the 32nd day to 1.0 mg. daily, and on the thirty-fourth day, when the serum Na^+ was found to be 164 mEq/l, to 0.5 mg. daily. At the same time the dose of potassium chloride was reduced to 2 g. daily.

The patient was allowed to return home on this regime. Though mentally somewhat depressed she was free of pain and was able to walk on her own with the help of a walking stick. Her condition improved steadily and she became much more cheerful. Radiological examination showed sclerosis in all the skeletal metastases except those in the ribs. It was hoped that it would be possible to control the maintenance therapy by regular estimations of the serum Na^+ and K^+, but this proved inconvenient owing to the fact that the patient lived a long way from the hospital, and it was decided to rely instead on 24-hour specimens of urine since these could be sent in without the patient herself being required to attend.

The patient continued to improve and on the seventy-ninth day the dose of fluorohydrocortisone was reduced to 0.4 mg. daily.

From about the ninety-third day her condition began to deteriorate and she complained of nausea and retching, pain of moderate severity in both subcostal regions, increasing weakness, loss of weight and a recurrence of the mental depression. The Na^+ and K^+ concentrations in the urine remained within normal limits and the only significant abnormal findings, apart from those already mentioned, were brownish pigmentation of the extensor surfaces of the forearms, and collapse of the 9th dorsal vertebra shown by radiological examination. The patient attributed her nausea and retching to the potassium chloride she was taking and decided to stop taking this salt. She became quite unco-operative but

TABLE 1 — METABOLIC STUDY (Mrs. V.T.)

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Day of Study	Maintenance Therapy (daily dosage)			Weight	Blood Pressure	URINE			SERUM		Fasting Blood Sugar	REMARKS
	Fluorohydrocortisone mg.	cortisone mg.	KCl g.	lb.	mm. Hg.	Volume ml.	Na^+ mEq./l.	K^+ mEq./l.	Na^+ mEq./l.	K^+ mEq./l.	mg./100 ml.	
1	—	—	—	121	120/80	700	67·5	50	150	4·1	100	
2	1·0	—	—	121	110/64	discarded	—	—	150	3·9	75	Right adrenalectomy
3	0·5	—	—	121	110/75	1030	25·0	65·0	—	—	—	
5	0·5	—	—	120	105/67	2300	2.0	9·1	148	3·7	90	
9	0·3	—	—	119	133/80	2060	19.4	13·4	140	3·6	105	
11	5·0	—	—	119	118/80	2650	23·0	16·5	—	—	—	
12	5·0	—	—	118	117/80	3200	13·2	16·3	160	3·9	95	Left adrenalectomy
13	4·0	—	—	—	100/68	215	3·0	44·4	158	4·0	125	
14	3·0	—	—	118	100/75	1640	1·5	37	146	3·8	100	
16	3·0	—	—	117	108/72	3200	0·17	9·4	151	4·32	—	
17	2·0	—	—	116	108/80	3860	0·48	10·6	—	—	—	
21	2·0	—	—	119	111/82	1890	4·1	23·2	142	4·8	70	
24	2·0	—	3	119	115/70	4080	2·2	17·5	—	—	—	
30	2·0	—	3	119	138/92	3590	11·6	16·6	147	3·0	70	
32	1·0	—	3	121	127/78	6700	20·4	17·0	—	—	—	
34	0·5	—	2	119	144/90	5400	16·8	19·2	164	4·0	60	
54	0·5	—	2	121	—	—	—	—	149·8	3·7	—	Discharged from hospital
75	0·5	—	2	122	148/92				145·0	3·9	—	
79	0·4	—	2	—	—	2100	37·5	39·5	—	—	—	At home
93	0·4	—	2	—	—	2360	40·5	35·5	—	—	—	
107	0·4	—	—	—	—	1800	28·5	23	—	—	—	
129	0·4	—	—	—	122/76	1525	36·5	30·5	147·0	4·1	45	Readmitted
135	1·0	—	3	—	136/80	2440	35·0	33·0	146·0	2·2	90	
138	1·0	—	3	112	—	2850	10·4	22·0	150·0	2·5	60	
142	1·0	—	5	112	116/74	3300	13·4	22·4	—	—	—	
144	1·0	—	7·5	112	—	2785	16·8	25·4	150·0	2·1	80	
145	0·5	10	10	112	—	2610	15·8	26·0	—	—	—	
149	0·5	10	10	—	130/90	3360	12·0	22·4	141·0	3·3	80	
152	0·5	10	10	111	122/88	1360	3·5	23·5	147·0	3·1	75	
153	0·5	10	10	—	—	3020	0·28	8·4	—	—	—	Discharged from hospital
164	0·5	10	10	—	—	2320	4·8	12·8	—	—	—	
165	0·2	40	10	—	—	—	—	—	—	—	—	
171	0·2	40	10	—	—	2360	25·6	19·0	—	—	—	
178	0·2	40	10	—	—	2290	18·4	23·6	—	—	—	
193	0·2	40	10	—	—	2160	24·0	15·8	—	—	—	At home
199	0·2	40	—	—	—	2300	36·0	24·8	—	—	—	
220	0·2	40	—	—	—	2360	26·0	21·5	—	—	—	
230	0·2	40	—	—	—	3080	30·0	16·5	—	—	—	
244	0·2	40	—	—	—	3000	25·0	10·25	—	—	—	
251	0·2	40	—	133	—	4440	30·0	17·7	—	—	—	
261	0·2	40	—	—	—	—	—	—	144·0	4·0	55	Readmitted for study
												Fluid intake (ml.)
262	0·2	40	—	—	—	4290	27·0	30·5	144·0	3·5	—	3660
263	0·2	40	—	—	—	4520	20·0	18·5	—	—	—	4170
264	0·2	40	—	129	146/90	4670	28·5	21·3	—	—	65	3960
270	0·2	40	—	129	124/80	4180	9·5	11·25	146·0	3·45	—	3780
279	0·2	40	—	—	—	4640	19·1	10·4	—	—	—	Discharged from hospital
286	0·2	40	—	—	—	4510	27·7	13·2	—	—	—	
300	0·2	40	—	—	—	3230	17·2	13·8	—	—	—	
307	0·2	40	—	—	—	3595	8·0	12·0	—	—	—	
314	0·2	40	—	—	—	2750	34·0	25·0	—	—	—	At home
325	0·2	40	—	—	—	3100	22·4	11·8	—	—	—	
335	0·2	40	—	—	—	3210	11·0	11·6	—	—	—	
342	0·2	40	—	—	—	3780	13.6	12·4	—	—	—	
353	0·2	40	—	—	—	3480	18·8	11·8	—	—	—	
374	0·2	40	—	—	—	3820	20·8	17·0	141·0	3·25	85	

after some persuasion agreed to return to hospital for reassessment, and she was re-admitted.

Electrolyte studies on the one hundred and twenty-ninth day revealed no abnormality but the fasting blood sugar was only 45 mg./100 ml. It appeared therefore that fluorohydrocortisone in a dosage of 0.4 mg. daily sufficed to maintain a normal electrolyte pattern but did not exert a sufficient glucocorticoid effect, and the dose was accordingly increased to 1 mg. daily. The blood sugar returned to normal but the serum K^+ fell sharply to 2.2 mEq/l and the patient's psychological state deteriorated still further. Since the hypokalaemia was the only abnormality in the electrolyte pattern it was decided to re-institute administration of potassium chloride. The dose, which was initially 3 g. daily, was increased to 5 g. daily and subsequently to 7.5 g. daily, but the serum K^+ remained dangerously low and it was concluded—somewhat tardily, perhaps—that it was not going to be possible to maintain the patient adequately with fluorohydrocortisone and supplementary potassium alone. Accordingly, on the one hundred and forty-fifth day of the study, the patient was given cortisone for the first time in a dosage of 10 mg. daily, and at the same time the dosage of fluorohydrocortisone was reduced to 0.5 mg. daily, and that of potassium chloride was increased to 10 mg. daily.

On this regime the serum K^+ increased to 3.3 mEq/l. The fasting blood sugar remained normal but after a week the urine once again showed evidence of marked sodium retention. As before there was no associated oedema or increase in weight. Although the patient was not properly stabilised she felt very much better and insisted on returning home. The sodium retention persisted and to correct it the dose of fluorohydrocortisone was reduced on the one hundred and sixty-fifth day to 0.1 mg. twice daily and at the same time the dose of cortisone was increased to 20 mg. twice daily, the total daily dose thus being 0.2 mg. fluorohydrocortisone and 40 mg. cortisone. On the one hundred and ninety-ninth day administration of potassium chloride was discontinued.

The patient continued to improve steadily. Her appetite and feeling of well-being increased, she began to put on weight, and she was able to walk increasing distances unaided and without pain. There was some return of thirst and polyuria but as far as could be judged from the urine specimens supplied, her electrolyte pattern was within normal limits; unfortunately, however, specimens were sent in at irregular intervals and sometimes were not complete 24-hour samples. She was re-admitted for full assessment on the two hundred and sixty-first day of the study. Her fluid intake was high and there was a corresponding degree of polyuria, but the serum Na^+ and K^+, and the fasting blood sugar, were found to be within normal limits. It appeared from radiological examination that the skeletal metastases had advanced somewhat, but a calcium excretion test (Jessiman and Moore, 1956) did not suggest that calcium was being mobilised from the bones. The patient was allowed to go home on the two hundred and seventy-ninth day and at the time of writing has been under observation for over one year. After her discharge from hospital, pituitary snuff was prescribed to see if this would control her polyuria. It appeared to be very effective but the patient never regarded the polyuria as anything of a disability and proved most uncooperative about taking the snuff, which had therefore to be discontinued. Her general health has remained remarkably well ever since. She has continued to receive 0.1 mg. fluorohydrocortisone and 20 mg. cortisone twice daily.

CONCLUSIONS AND DISCUSSION

Many adrenalectomised patients cannot be maintained adequately on cortisone alone. It seemed to us possible when this study was started that fluorohydrocortisone alone might provide satisfactory steroid replacement but it was found that, whereas with cortisone the mineralocorticoid effect is insufficient in comparison with the glucocorticoid effect, with fluorohydrocortisone, as Hart (1956) and others have also found, the mineralocorticoid effect is far too great. It seemed logical therefore to use both these hormones in combination, and in the case presented satisfactory maintenance was achieved by giving 0.1 mg. fluorohydrocortisone and 20 mg. cortisone twice daily. It is of interest that de Gennes *et alii* (1956) have recently reported that these two hormones in combination provide the most satisfactory steroid replacement therapy in patients with Addison's disease.

It seems likely that the amount of each steroid required after surgical adrenalectomy will vary from patient to patient. It would seem also that in the presence of intercurrent

infections or diarrhoea the dosage would need to be increased. Our experience suggests, however, that once the patient is properly stabilised the dose schedule in the absence of complications will require little alteration.

Since cortisone and fluorohydrocortisone are effective when given by mouth the patient is not greatly inconvenienced by having to take both. It would however mean a considerable simplification, though at the cost of some loss of flexibility, if the effect obtained with a combination of steroids could be achieved with a single steroid, and it is pertinent to ask whether this is likely to be possible. Several halogenated steroids have now been synthesized and one of these, 1-dehydro-9α-fluorohydrocortisone is about three times as powerful as fluorohydrocortisone as a glucocorticoid and about one and a half times as effective as a mineralocorticoid (Fried, 1956). We have not used this substance but it would appear to be nearer to what is required than fluorohydrocortisone but still relatively deficient in its glucocorticoid action. It seems reasonable to expect, however, that as new steroids are produced, one will be found which has the required properties.

SUMMARY

Neither cortisone nor 9α-fluorohydrocortisone acetate alone provides adequate steroid replacement in adrenalectomised patients: cortisone because its mineralocorticoid action is insufficient in comparison with its glucocorticoid action, and 9α-fluorohydrocortisone acetate because the converse is true. By using both these steroids a proper balance can be achieved. One patient, who has been studied in detail for a year following bilateral adrenalectomy, is being satisfactorily maintained with 0.1 mg. 9α-fluorohydrocortisone acetate and 20 mg. cortisone twice daily by mouth.

ADDENDUM

Since this paper was submitted for publication three more patients have been subjected to bilateral adrenalectomy. It appears that in the patient we have reported in detail the corticoid dosage at the time of the adrenalectomies was somewhat excessive. For this reason the standard dosage we now adopt is as follows: *First Adrenalectomy* (combined or not with oophorectomy): no corticoid replacement under careful supervision during the post-operative period. *Second Adrenalectomy:* 0.1 mg. fluorohydrocortisone and 20 mg. cortisone on the evening before the operation; 0.4 mg. and 80 mg. respectively in divided doses on the day of the operation; 0.2 mg. and 80 mg. respectively on the second post-operative day; 0.2 mg. and 40 mg. respectively on the third post-operative day; 0.2 mg. and 30 mg. respectively from the fourth day onwards. Slight re-adjustment of this dosage may be required and this is determined by the clinical state of the patient and by periodical estimations of the Na^+/K^+ ratio in 24-hour collections of urine and of the fasting blood sugar.

If, at the time of the first adrenalectomy, it is suspected that the patient has adrenocortical metastases which have resulted in impaired cortical function it is advisable to administer 0.2 mg. fluorohydrocortisone and 30-40 mg. cortisone from the day of the first operation, because of the risk of producing acute adrenocortical deficiency if the gland removed happens to contain the bulk of the patient's functioning cortical tissue. After the second adrenalectomy the dosage is changed to conform to the standard described above.

ACKNOWLEDGEMENT

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CHANGES IN CELLULAR PROTEINS DURING CHEMICALLY-INDUCED TUMOUR FORMATION IN THE LIVER

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AN understanding of the nature of cancerous growths has always been an important biological goal: the fundamental features of this apparently aberrant process are bound up with those of the normal control of growth in the individual in which the tumour develops. The recent increasing recognition of the ineffectiveness of all therapeutic methods of attack, as far as cure of most neoplasms is concerned, has focussed attention even more strongly on the fundamental processes involved in tumour development.

An important weapon in this attack on the aetiology and pathogenesis of cancer, developed in the last three decades, has been the recognition of many chemical carcinogens whose effects may be studied from the time of their introduction into the body until and after the development of the tumour.

Some of the observations which have been made by the experimental use of one of these —4-dimethylaminoazobenzene—on the liver of rats and certain conclusions which may be drawn from these are presented here.

Historical

There are here two different and distinct aspects of the problem of carcinogenesis: first the role of the long appreciated but belatedly demonstrated chemical substances which give rise to tumours of various kinds and secondly, the question of the nature of the fundamental difference between the cancer cell and its normal prototype.

Chemical carcinogens were first indicated, even though in a primitive and ill-defined fashion, by Percival Pott in the 18th century when he noted the relation of scrotal tumours of chimney-sweeps to soot. It required nearly 200 years to unveil benzpyrene and other condensed polycyclic hydrocarbons derived from coal tar. Although this group is of fundamental importance and has the prestige and priority of eldership and tradition, other chemical substances have gradually assumed an important and, in many cases, a unique place in the general chemical group. The azo dyes show some special features which are discussed here.

Fischer (1906) noted the formation of atypical epithelial growths, which histologically resembled cancers, in the ears of rabbits following the injection of scarlet red. Unlike cancers, however, these growths invariably receded when the chemical stimulus was removed. Yoshida (1933) showed that o-aminoazotoluene, which is part of the scarlet red molecule, is capable of causing these effects. When fed to rats on a rice diet at a level of 1 mg. of dye per g. of food for two months, it induces the formation of hepatomata or cholangiomata in all rats which survive more than 255 days. Kinosita (1936) reported that 4-dimethylaminoazobenzene is a much more active hepatic carcinogen for rats than o-aminoazotoluene.

Further work has shown that the carcinogenicity of this dye is dependent upon a restricted riboflavin intake. Of species so far tested only rats and mice are susceptible to the carcinogenic action of 4-dimethylaminoazobenzene and the primary tumours have been confined almost exclusively to the livers of these animals. Miller and Miller (1947) reported that, in the livers of rats and mice fed the dye, a derivative of the dye could be demonstrated to be firmly bound to one or more of the liver proteins. This bound dye was not liberated by prolonged boiling with a variety of organic solvents and could only be recovered after hydrolysis of the protein. They found that, coincident with tumour development, there was a loss of the capacity to bind the dye by the tumour nodules but not by the surrounding liver tissue.

Regarding the nature of malignant disease, it has always been tacitly assumed that the growth was something essentially different from the surrounding tissues—some kind of parasite.

When the concept of immunity began to develop in the last century, especially regarding infecting organisms, it is understandable that the idea should have been applied to tumours and, indeed, this began early on an experimental basis.

The suggestion was made that, following an injection of tumour tissue into another animal, an antiserum could be obtained. When injected into the individual with the tumour, reaction of the antiserum with the proteins of the growth should occur with possible destruction of the growth. However, from the first attempt (Héricourt and Richet, 1895), which was followed by many others, this has been invariably fruitless. The reason for this, which has taken decades to be thoroughly realized, is that a tumour is essentially part of the body—the tumour cells are body cells—and in these experiments there is produced "not an anticancer but an antiman serum" (Oberling, 1944).

Many difficulties were encountered in the production of cytotoxic sera and in 1910 Roessle concluded from the available literature and his own work that they could not be effectively produced. However, Masugi (1933) demonstrated that this was merely a question of producing a sufficiently large dose of the serum.

The complexities of the matter were demonstrated by Lumsden (1931) when he showed that effects not apparent on the cells in the body could be seen when cells were treated with antiserum *in vitro;* the converse was most important—that effects produced on cells *in vitro* would not necessarily be produced in the body.

That immunity could be produced against transplanted tumours was shown by Besredka and co-workers (1936) when they immunized rabbits against a transplantable carcinoma (the Brown-Pearce tumour) and subsequently Saphir and Appel (1940) showed that grafts of tumour into the skin of animals with well-developed growths were followed by disappearance of the tumour and even of metastases. However, this kind of observation has never yet been found to apply to naturally-occurring neoplasms. Many years ago, at the crest of the wave of the new immunological knowledge, Ehrlich (1907) despondently remarked that "until some fundamental discovery has solved the mystery of life itself our knowledge of cancer will not advance a single step".

Thus, from the unjustified hope that the original crude immunological methods would provide a therapeutic agent for cancer, through an era of increasing appreciation of the complexities of the problems involved, investigators have now come to a more objective approach to these phenomena and much more precise and therefore more significant observations are being made.

FIG. I. Graph showing level of protein bound dye in rat liver at different stages of feeding estimated spectrophotometrically. The descending limb of the curve may be correlated with diminution and loss of a protein which binds the dye.

When specific antibodies, produced by the injection of a tissue into another animal, are introduced into the original animal, the antibodies react with the corresponding antigens of the particular organ. These do not necessarily produce the gross changes that were expected by investigators in the early part of the century, but their presence can be demonstrated by the use of fluorescing dyes which combine with the antibodies. Since the antibodies are fixed in the cells, and indeed in certain parts of the cells, the site of the antibodies and the original antigens can be determined (Coons and Kaplan, 1950; Coons, Leduc and Kaplan, 1951; Marshall, 1951, 1954; Hill and Cruickshank, 1953; Gitlin, Landing and Whipple, 1953; Clayton, 1954).

This may be correlated with the observation mentioned above that certain proteins of the cells combine with the azo dyes and it is these proteins which probably incite the production of antibodies.

By means of observations with these fluorescing dyes it has been shown that the cells of tumours lack specific proteins which stain with the dyes and this again may be correlated with the absence of the proteins which bind the azo dyes. These observations appear to be providing at least the beginnings of an answer to the possible differences between one kind of cancer cell and the corresponding normal cells of the body.

(2) Fluorescence Antibody Studies—Using a fluorescence antibody technique, Weiler (1952, 1956) has reported the loss of a cell component, which has been designated an "organ specific antigen", during aminoazo dye carcinogenesis in rat liver. In 1954 he presented confirmatory serological data.

Mitochondrial and microsomal fractions of rat liver homogenates were prepared, using

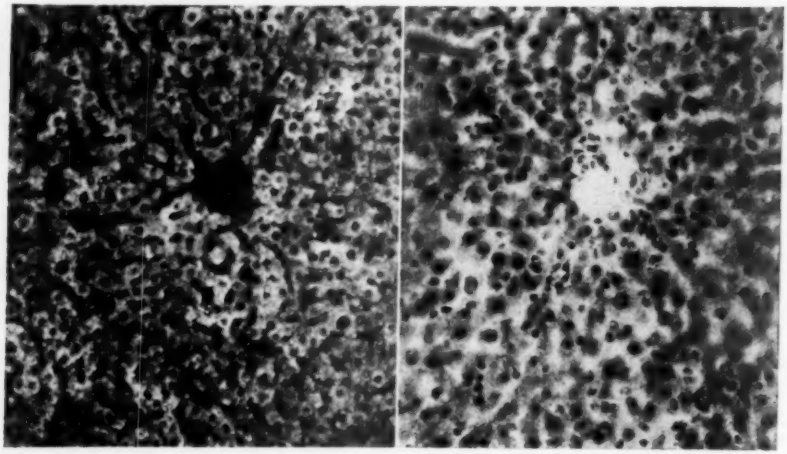

FIG. II FIG. III

FIG. II. Photomicrograph of a frozen section of normal rat liver stained with fluorescent serum. The liver cells stain uniformly. (x 120)

FIG. III. Photomicrograph of a section of normal rat liver serial with that shown in Fig. II and stained with haematoxylin and eosin for comparison. (x 120)

OBSERVATIONS

(1) Adult Sprague-Dawley-Holtzman rats were fed a semi-synthetic diet containing 0.06 per cent. 4-dimethylaminoazobenzene and 2 mg. of riboflavine per kg. of diet for ten to twelve weeks. At the end of this period the livers of the rats were grossly cirrhotic and contained numerous tumour nodules. Some of the animals showed metastases. The tumours histologically could be classified as hepatoma or cholangioma. Often the same tumour showed areas exhibiting both histological pictures.

Animals were sacrificed at fortnightly intervals during dye feeding and spectrophotometric estimations of the protein bound aminoazo dyes were performed using the method of Miller and Miller (1947); the level of bound dyes was found to agree with the findings of Miller and Miller (Fig. I).

sucrose media, by differential centrifugation and were used as antigens by injecting them intravenously into rabbits over a period of three to four weeks. A globulin fraction of rabbit serum, prepared from rabbits showing a satisfactory titre of antibody to complement fixation test, was then coupled with fluorescein isocyanate using the method of Coons and Kaplan (1950); the resulting serum was absorbed several times with particulates prepared from rat kidney. This serum was then used as a histoserological stain on unfixed frozen sections of (i) rat liver, (ii) liver undergoing carcinogenesis and (iii) liver tumours. The sections were examined using a fluorescence microscope. The normal liver tissue stained uniformly with fluorescent materials (Fig. II) but tumours of the liver both hepatomata (Fig. IV) and cholangiomata (Fig. VI) failed to stain in this manner.

It is found that during carcinogenesis there is a progressive diminution of fluorescence, which Weiler interpreted as a loss of "organ specific antigen", from nests of liver parenchyma. However, it has been found that a fluorescent globulin fraction of serum prepared from untreated rabbits gives identical differential staining and therefore such staining is independent of the presence of fluorescent antibodies to rat liver.

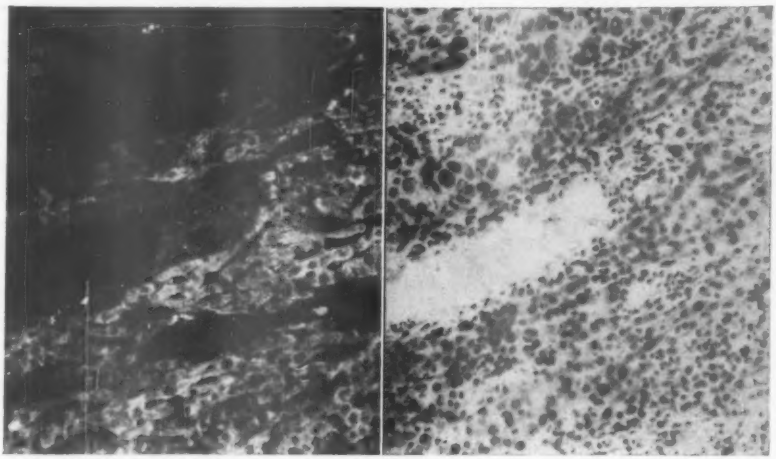

FIG. IV FIG V

FIG. IV. Photomicrograph of a frozen section of a rat hepatoma stained with fluorescent serum. Normal cells stain but neoplastic cells do not. (x 120)

FIG. V. Photomicrograph of a section of the rat hepatoma serial with Fig. IV, stained with haematoxylin and eosin. The structure of the malignant tissue (non-staining in Fig. IV) is shown. (x 120)

DISCUSSION

From the above observations a tentative hypothesis regarding a process of possible causal significance in aminoazo dye carcinogenesis may be presented.

Studies of protein bound dye by Miller and Miller (1947) in several animals showed that binding of dye occurs only in mice and rats. Incidentally, these are the only species in which the dye has been demonstrated to be carcinogenic. Furthermore, the bound dye is detectable only in the livers of these animals —the only site where the dye is carcinogenic. Using a variety of animoazo dyes they have found that the time taken for the development of a maximum level of dye binding is directly proportional to the carcinogenicity of the particular dye. The tumours themselves have no capacity to bind the dye. Miller and Miller suggest that the dye interferes with the re-synthesis of growth controlling protein(s) in the liver cell and ultimately causes a cell race to arise without this protein. The ascending portion of the dye curve (Fig. I.) would represent a period when the liver is synthetizing the dye-binding protein more quickly than the dye is causing its deletion and the descending portion of the curve would represent a period when the rate of deletion is the greater; this leads to the ultimate development of cells lacking this protein and hence without the ability to bind the dye, that is to say, cells which are different in one respect only but which difference is, in some way, related to a capacity for continuous growth.

The fluorescence staining studies clearly demonstrate, coincident with carcinogenesis, the loss or modification of a cytoplasmic constituent, with an affinity for derivatives of fluorescein isocyanate, in the liver parenchymal cells. The aminoazo dye, being a tissue-damaging agent, would excite considerable cellular proliferation of liver cells so presumably the discrete islands of cells showing loss of this specific liver protein would arise from proliferation of cells showing this

loss. Thus, from two different approaches, evidence can be found that during aminoazo dye carcinogenesis of rat liver there is either a loss or a modification of a liver protein whereby the cell loses the capacity to bind the carcinogen and the ability to stain histoserologically with a fluorescent dye.

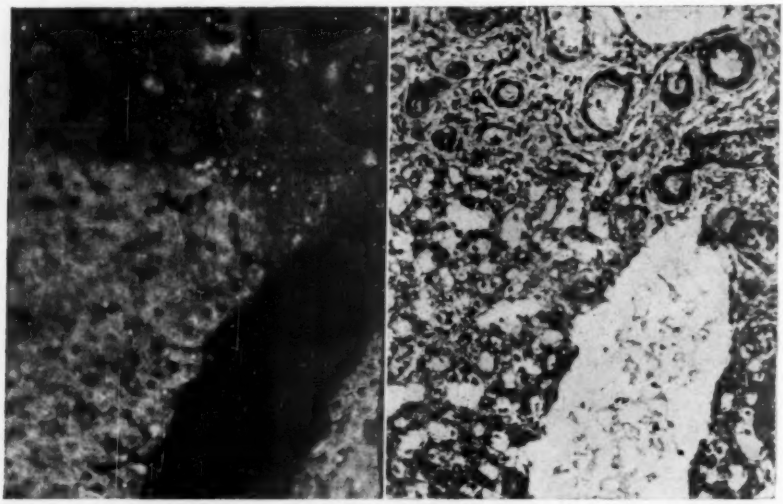

FIG. VI FIG. VII

FIG. VI. Photomicrograph of a frozen section of a rat cholangioma stained with fluorescent serum. Normal cells stain but tumour tissue does not. (x 120)

FIG. VII. Photomicrograph of a section of the rat cholangioma, serial with Fig. VI and stained with haematoxylin and eosin. The structure of the tumour (non-staining in Fig. VI) is shown. (x 120)

To what extent this represents a significant stage in the causal mechanism in carcinogenesis is still uncertain but it points to the attractive speculation that the cell is cancerous because it has lost a specific cellular protein by which the body can control its growth. That here we have a demonstrable difference between the normal and the cancer cell is indisputable. These observations are a long way from any clinical application but any step towards the understanding of the neoplastic process (and seems to be a definite one) is of potential practical import.

SUMMARY

Evidence is presented that in the malignant cell of rat liver tumours a highly specific cellular protein has either been lost or has been modified; this is judged by the cell's inability to bind a metabolite of carcinogenic aminoazo dye or to react with a fluorescent dye. It is suggested that through this loss or modification, which is permanent and is transmitted to its progeny, the growth of the resulting cell race is uninfluenced by the various organizing factors which normally control the growth of tissues and organs and, in ordinary circumstances, limit the proliferation of tissue cells.

The significance of these observations in human neoplasms is as yet uncertain. However, this is being studied and if the staining technique should prove applicable it will be not only a valuable method of investigating tumours but possibly also important in differentiating tumour-like masses from true neoplasms.

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PRIMARY REPAIR OF COMPLETE RUPTURE OF THE DEEP URETHRA

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Introduction

THIS article is concerned only with complete rupture, or rupture-dislocation of the deep urethra, and not with lesser injuries. The condition is uncommon and often associated with multiple injuries. Always, except in the case of missile injuries, it is associated with some type of fracture of the pelvis.

A recent article by Quick (1956) discusses methods of secondary repair of these injuries treated primarily by the traditional method of catheter splintage. The purpose of this article is to present a case repaired by the retropubic route and to contrast it with cases treated by the traditional method. The condition concerns the general surgeon dealing with emergencies as well as the urologist. The division of these rare cases tends to restrict individual experience.

Cases Treated by Standard Method

The writer's experience of the results of treatment by the standard method is limited but unsatisfactory. For example, a boy of two awaits, with a suprapubic drain, treatment for the stricture which has replaced the gap left by failure to achieve apposition of the two ends of the urethra.

Also, a young man, treated by a competent surgeon with the usual method, came under treatment eighteen months later. His condition, following infection and failure to close his gap was as shown in Fig. I.

He had:—

1. A transverse colostomy, later changed to a left iliac colostomy.

2. Fistulae and a gap of about 2½ inches. These fistulae were as seen in Fig. 1.

3. A solid block of tissue resulting from infection in his persisting dead space.

His present condition is that his thigh fistula has closed with prolonged suprapubic drainage, and surgical treatment has closed his scrotal fistula but has failed to close his recto-urethral fistula. He is continent and in good general health, but the future plans for this patient require some thought.

FIG. I. Showing (A) Contrast medium in recto-sigmoid.
(B) Recto-"urethral" fistula.
(C) Fistula to right thigh.
(D) Fistula to scrotum.

Repair by Retropubic Route

The problems of primary repair appear to be:—

1. The elimination of the gap which may be up to 3 inches between the ends of the urethra. "Catheter splintage", on retropubic examination of the pelvis, does not allow

accurate apposition of the two ends. The dislocated proximal urethra, prostate and bladder may be found floating on an extra peritoneal collection of blood and urine, or if this is small, will be found grossly displaced upwards and backwards with the bladder and prostate acutely "anteverted".

2. The prevention of infection, extravasation, and persisting dead space from failure to restore the normal anatomy.

It is realised that no firm conclusions can be drawn from individual cases, but a single case primarily repaired is described:

1. Because there seems to be no literature of note on the subject, although Terence Millin suggests the approach in his book.

2. Because the patient concerned gave an opportunity to examine the join in his urethra by having a fatal coronary thrombosis some two months after repair.

Perineal repair does not appear to be the answer to the problem.

It is also realised that other types of retropubic primary reconstruction must have been done and not recorded.

Case History

Patient aged 69. Run-over accident.
Findings On Examination:

(a) A severe tension pneumothorax threatening his life on admission.

(b) A fractured left humerus.

(c) Multiple rib fractures.

(d) A fractured pelvis with blood at the external urinary meatus and, on rectal examination, the prostate replaced by a soft fluid mass.

Treatment: His tension pneumothorax was relieved by intercostal catheter and suction. Resuscitation with whole blood was carried out and preparations made for reconstruction of his urethra.

Operative Procedure:

1. Incision — a skin crease incision across the lower abdomen, two fingers above the pubis, dividing both rectus muscles and splitting the obliques after ligature of both deep epigastric arteries.

2. Exposure and haemostasis by packing and ligature aided by the light of a cystoscope. Blood loss was surprisingly easy to control. The retropubic space was exposed in the usual way and using the light of the cystoscope as an additional aid, the exact position of affairs was easily assessed.

3. Restoration of bladder and prostate to normal position.

(a) A curved metal sound was passed through the prostate and the bladder examined after restoring it to its normal position.

(b) As the bladder was severely bruised, it was considered wise to make a one inch incision in the anterior wall and substitute for the metal sound, the curved forceps shown in Fig. II, to maintain the position of bladder and prostate while the stay suture was inserted.

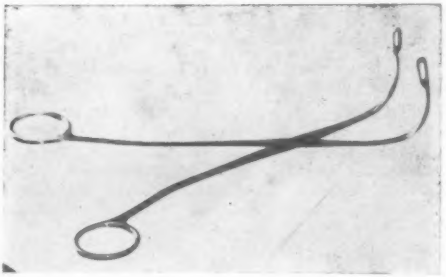

FIG. II. Forceps used to support bladder and prostate while stay suture is inserted. (If opening of the bladder is considered advisable.) If the bladder is not opened it can be held up in position by a curved sound through the prostate.

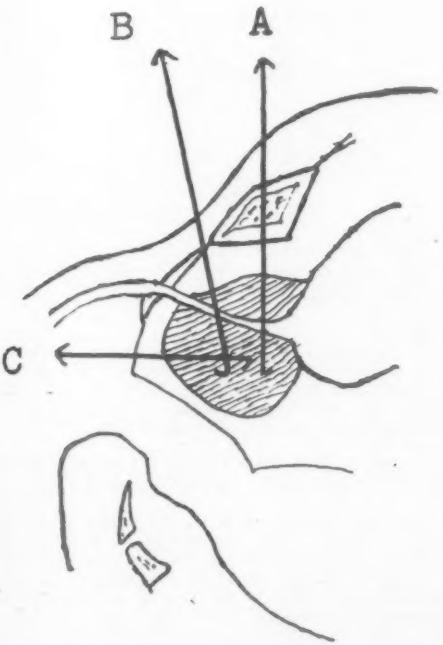

FIG. III. Possible directions for stay sutures:

A. Suprapubic—forwards and slightly downwards.
B. Perineal—forward and downward.
C. Perineal—downward.
A combination may be used.

(c) A stay suture was passed as shown in Figs. III and IV. The suture material was of strong nylon and was brought out on each side of the pubis as a forward and slightly downward pull was required in this case to maintain position. The stay suture was tied through a piece of rubber tubing hooking over the skin over the pubis. Perineal stay sutures were contemplated but were found unnecessary as this prostatic stay suture maintained perfect position.

(d) A Foley catheter was drawn into the bladder with the curved forceps after withdrawal of cystoscope.

(e) Suture of the urethra was found to involve only two or three fine catgut stitches as the ends of the urethra fell into exact apposition over the catheter. Closure of the small hole in the bladder was done in the usual way after inspecting the bladder for further tears and emptying it of blood clot.

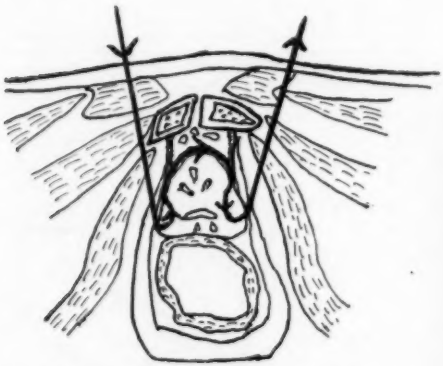

FIG. IV. Transverse section of the pelvis to show the use of a single stay suture through the lateral lobes of the prostate, which produced accurate reduction of the rupture dislocation described.

4. Drainage and closure. Three drains were inserted, one to the join and one to each side of the prostate, and the abdominal wall closed with interrupted thread. This patient was operated on in his bed, the bed being draped as an operating table.

After treatment: The catheter was removed in 10 days. The stay suture was removed in 3 weeks.

Progress: There was a normal stream from the time of removal of the catheter and a sound passed without obstruction; rectal examination was normal; the patient was up and about with a stable fracture of the pelvis; eight weeks later he suffered a fatal coronary thrombosis.

Post-mortem: The pelvis was found to be clean and it was extremely difficult to find, in the urethra, the join which resembled a fine thread in its wall.

Radiological results: Bedside cystourethrograms were done and are shown together with comparable films of an uninjured patient (Figs. V, VI). True lateral cystourethrograms, which unfortunately will not reproduce, showed identical alignment in injured and control cases.

FIG. V. Cysto-urethrogram of repaired case.

FIG. VI. Cysto-urethrogram of an uninjured patient.

CONCLUSION

A method of simple retropubic primary repair of the ruptured deep urethra is described because of the lack of literature on the subject and because it is felt that some such simple method is possibly worthy of a trial as a standard method, the results of older methods appearing often to be unsatisfactory, and having in view the very grave problems associated with secondary repair.

Since this paper was written, the case quoted above with multiple fistulae, three years after injury, has been repaired by a synchronous retropubic-perineal operation. It was found to be possible to restore the urethra to its original position using both "anterior"

prostatic stay sutures and "perineal" "downward" stay sutures, and to excise the recto-urethral fistula. His perineal wound was left open and was lightly packed and the retropubic dissection, which was not easy, combined the above stated principle with the "ruthless excision" of Winsbury-White applied to the scar tissue block behind the pubis. It is too early yet to give an opinion on the prognosis of the case but exact apposition of the urethra was secured, the alignment of the urethra is normal, there are no fistulae, and micturition is performed with good stream and full control.

ACKNOWLEDGEMENTS

My thanks are due to Dr. Graeme Sim for his radiological help, to Dr. Neville Dorrington for his skilled anaesthesia, and to Mr. Hamblyn for the photographs.

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SOLITARY DIVERTICULUM OF THE CAECUM

A REPORT OF THREE CASES

By Neil Johnson

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AMONGST the diseases which may simulate acute appendicitis in their clinical manifestations is the uncommon lesion of acute inflammation of a caecal diverticulum. Correct pre-operative diagnosis is so seldom made that the surgeon, having explored the right iliac fossa, finds himself confronted with an unusual caecal mass and a normal appendix. Accurate assessment of the operative findings is important in that appreciation of the true basis of the lesion may save the patient from the morbidity and mortality of an unnecessarily radical operation.

Interest in this condition was stimulated by personal experience of the first case reported in this paper. Two further cases treated by simple excision were found on a survey of the records of the Royal Melbourne Hospital over a period of sixteen years — from 1940 to 1956, and during the same period two solitary diverticula were detected at routine post-mortem examination on the patients dying of unrelated conditions.

Case Reports

Case 1

Mrs. E.M., aged 27, was admitted to hospital with a three-day history of abdominal pain. Initially central abdominal in site, it had moved to the right iliac fossa twenty-four hours before admission and had persisted there since that time; there was associated vomiting but no other symptoms.

Examination revealed the patient to be a healthy young woman with a temperature of 99.8° and a pulse rate of 90. The relevant physical findings were limited to the abdomen, where localized deep tenderness was present in the right iliac fossa. There was no release tenderness or rigidity and Rovsing's sign was negative.

A clinical diagnosis of acute appendicitis having been made, the abdomen was opened and a normal appendix found. However, an irregular firm mass, 4 x 5 cms. in diameter, was detected in the postero-medial part of the caecum. Palpation revealed a chain of enlarged lymph glands continuous with this mass and extending along the ileo-colic artery. On the mucosal aspect of the main mass there was a smooth, hard, circular swelling, 1.5 cms. in diameter; its significance was not appreciated until the specimen was examined post-operatively. These findings lead to an operative diagnosis of carcinoma of the caecum and a right hemi-colectomy was performed. The patient made an eventful recovery but suffered from a mild attack of sub-acute small bowel obstruction three months post-operatively. This episode subsided with conservative management.

Examination of the specimen showed the diagnosis at operation to be incorrect. An acutely inflamed solitary diverticulum was found at the level of the upper edge of the ileo-caecal valve and continuous with this an indurated inflammatory mass extended into the postero-medial part of the caecal wall. A faecolith in the cavity of the diverticulum accounted for the regular smooth swelling detected at operation (Fig. 1).

Case 2

A 69-year-old man was admitted to hospital with a seven-day history of generalized abdominal pain becoming localized in the right iliac fossa during the forty-eight hours prior to admission. He had vomited on two occasions during this period.

Examination revealed a man, robust for his age, with the main physical abnormalities being limited to his abdomen. The signs there were consistent with a diagnosis of acute appendicitis and the right iliac fossa was explored through a McBurney's incision. Operation revealed a normal appendix and a mass involving the antero-lateral aspect of the caecum. Palpation of the mucosal surface of the mass through the opposite caecal wall revealed the orifice of the diverticulum; mis-interpreted at that time as the edges of a neoplastic ulcer. A diagnosis of carcinoma of the caecum was made and the McBurney's incision was closed. Ten days later, at second laparotomy, it became apparent that the mass was, in fact, an inflamed diverticulum. Complete and uneventful convalescence followed local excision of the diverticulum.

Case 3

A 69-year-old woman was admitted to hospital following a two-day history of pain starting in the right iliac fossa. Her pain had started gradually and increased steadily in severity since onset. There were no further associated symptoms.

Examination revealed a rather frail woman with a temperature of 99.4° and a pulse rate of 100. Abdominal palpation showed localized deep tenderness over the caecum and a pre-operative diagnosis of acute appendicitis was made. However, on delivering the caecum by McBurney's incision an inflamed solitary diverticulum was found on its antero-lateral aspect, the appendix being normal. The diverticulum was excised locally, the appendix removed and the abdomen closed. An uneventful convalescence followed and the patient was discharged well on the seventh post-operative day.

DISCUSSION

Accurate assessment of the rate of incidence of diverticulitis of the caecum is virtually impossible. Many cases of this unusual conditions seen at operation fail to be recorded in the literature and it is highly probable that more are masked when a diagnosis of "appendix mass" is made and conservative treatment embarked upon (Reid, 1951).

The first recorded case of inflammation in a solitary caecal diverticulum is that of Potièr (1912). Since that time single cases and groups of cases have been sporadically reported (Gabriel, 1937; Abel, 1938; Gordon-Taylor, 1938). By 1937 Bennet Jones was able to collect and review 17 examples of the condition and ten years later Anderson (1947) collected 99 case records and used them as a basis for an excellent review. It would appear that about 1 per cent. of cases of diverticulitis of the colon as a whole occur in the caecum (Mayo, 1950). The fact that the diverticulum in the caecum may be the only demonstrable large bowel lesion and that complications occur in these caecal diverticula at a much earlier stage than is seen elsewhere leads one to suspect that they have a different aetiology from that of the more commonly seen diverticula of the left side of the colon.

Various suggestions have been put forward to explain these lesions, 80 per cent. of which occur in the bowel wall immediately above or below the level of the ileo-caecal valve. The ingenious postulate that they represent a misplaced Meckel's diverticulum would appear untenable since Odqvist and Petren (1931) described the co-existence of these lesions in a child aged three. That some may follow damage to the caecal wall by the trauma of appendicectomy has been suggested by Jemeren (1952). The idea that a diverticulum may follow destruction of the muscle coat of the caecal wall by acute non-specific ulcer is an attractive one, but appears to have little evidence to support it. To label the lesions congenital is merely to hide our ignorance behind a word.

The diverticulum usually contains a faecolith and when inflammation supervenes the range of possible sequelae is the same as are observed to occur in the more common left-sided diverticulitis. The risk of perforation would appear to be not so great as it is on the left side, though it has been reported (Updegrove, 1955).

The correct pre-operative diagnosis of this condition is practically impossible in a patient who has had no previous surgical interference. Whilst on statistical grounds it has been estimated that the story of vomiting is less frequent in caecal diverticulitis than it is in acute appendicitis, this information is of little value in the particular case (Kirkman, 1950).

FIG. I. Photograph of the operative specimen obtained from Case 1. The caecum, ascending colon and terminal ileum, together with the peritoneum about the ileo-colic and right colic arteries are seen. A smooth, finger-like projection is seen to occupy the postero-superior section of the ileo-caecal valve. The apex of this projection has been cut away (in a roughly rectangular fashion) to show a faecolith in the diverticulum, whose orifice can be seen just below and to the right of the cut away area. Inflammatory changes extended from this diverticulum out into the posterior wall of the caecum. Note the enlarged lymph node at the site of ligation of the right colic artery.

Even at operation the correct pathological assessment is uncertain — Laurisden and Ross (1952) reported a mis-diagnosis as carcinoma in 30 per cent. of 153 cases subjected to laparotomy: this error being one which may befall even the most experienced of surgeons.

Diverticula presenting on that part of the wall of the caecum and ascending colon which are covered with peritoneum are usually easily recognized, providing that the condition is given consideration at laparotomy. Those situated on the bare area of the caecum, particularly if they be associated with extensive inflammation, may mimick carcinoma with considerable accuracy. Where possible local treatment should be directed towards the diverticulum. Laurisden and Ross in their review have shown that right hemi-colectomy bears a much higher mortality than does local excision. It would seem that simple excision of the diverticulum is the treatment of choice in most cases. Inversion of the diverticulum and suture of the caecal wall, as suggested by Vaughn and Narsete (1952) is a less satisfactory procedure.

Di Fiore (1952) and Cave and Shea (1953) have reported cases, diagnosed at laparotomy and treated conservatively after closure of the abdomen. Such an inactive approach with the accompanying risk of recurrence of symptoms would appear unnecessary in these days of adequate antibiotic cover. Occasionally, in the presence of much local induration in the surrounding caecal wall, a caecostomy through the diverticulum, as advocated by Frehling (1952) may be the method of choice, but it is difficult to agree with this author's suggestion that most cases should be treated in this fashion.

In any group of patients right hemicolectomy always figures high on the list of therapeutic procedures adopted for caecal diverticulitis (Schnug, 1943; Byrne *et alii*, 1950). Mis-diagnosis as caecal carcinoma accounts for the prevalence of this operative procedure. However, as Jonas (1940) pointed out, a resection is necessary when the diverticulum encroaches on the ileo-caecal valve because of the impossibility of local excision of the lesion.

SUMMARY

1. Three cases of diverticulitis of the caecum have been reported.
2. A brief survey of the literature has been given.
3. It is pointed out that, provided the condition is thought of, a high percentage of correct diagnoses should be made in those cases where the diverticulum is in the peritonealized area of the caecum.
4. A common diagnostic error is that of regarding the lesion as a carcinoma. This will occur particularly when the lesion is situated on the posterior aspect of the caecum or ascending colon.
5. A simple excision of the diverticulum is the treatment of choice.

ACKNOWLEDGEMENTS

I wish to thank the staff of the Royal Melbourne Hospital for permission to review the hospital records and to use the history of the cases described in this paper. I am also indebted to Mr. R. Inglis, Clinical Photographer to the Royal Melbourne Hospital, for the excellent photograph of the specimen shown in Fig. I.

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CYSTADENOCARCINOMA OF THE PANCREAS

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NEOPLASTIC cysts of the pancreas are rare and usually provide difficulty in diagnosis. Malignancy in these cystic lesions is even more unusual. The following case showed features indicating these changes, and in addition provided problems in diagnosis clinically and at laparotomy, before the nature of the lesion was determined.

Case Report

Miss M.Y., aged 45, was admitted to the Dunedin Hospital on 12th February, 1953. The patient was mentally subnormal and gave a poor account of herself. Her chief complaint was that of increasing abdominal distension, which the patient insisted had been present for only a few weeks. A relative stated that she had complained of it for two years. During the four days before admission, mild abdominal pain had developed, and she had vomited on several occasions. Her appetite had remained good up to the day of admission and she had not been confined to bed.

On examination, there was obvious ascites, and paracentesis was performed, 32 pints of fluid being aspirated. After this procedure, an enlarged spleen was thought to be present but no other abnormal masses were detected. Ascites gradually recurred, and it was decided to perform a laparotomy.

On 10th March, 1953, the abdomen was opened by a transverse upper abdominal incision. A large quantity of blood-stained fluid was found in the peritoneal cavity. A cystic mass was found in the transverse mesocolon, and this was adherent to a loop of bowel. No plane of cleavage was found, and a solid portion of the mass was removed for pathological examination. Blood clot and gelatinous material oozed from the centre of the mass. The abdomen was closed and a pint of blood was given post-operatively.

Histologically, the fragment examined showed a lining composed of tall, regular, columnar secretory epithelium arranged in a single layer. There was abundant mucinous material. The appearances were those of a pseudomucinous cystadenoma.

The patient's condition remained fair. Ascitic fluid was removed on 14th March and her condition steadily improved. In view of the histological report it was decided to conduct a further exploration of the abdomen.

This was done on 31st March, the operation being preceded by a transfusion of two pints of blood. A transverse upper abdominal incision was again used. The cystic mass was found to originate in the pancreas. With some difficulty, planes of cleavage were found and the mass gradually enucleated from the lower surface of the transverse mesocolon. The adherent loop of jejunum was torn during separation, and this was closed by suturing. The patient was in good condition when the abdomen was closed. She made an uneventful recovery, and was discharged on 22nd April, 1953. There was no recurrence of the ascites at this time. When last seen in November, 1956, the patient was in excellent health, and examination revealed no abnormality in the abdomen.

FIG. I. Photograph of the operation specimen showing interior of bilocular cyst. Solid, fleshy growths project into the cavity.

Pathological report

The specimen was a thick-walled cystic mass weighing 160 gms. and measuring 7 cm. in diameter. The interior was comprised of two locules, from the walls of which numerous fleshy growths projected into the cavity. There was a considerable quantity of blood clot present (Fig. I).

Histological study showed that the cyst was lined by a tall columnar epithelium having a marked papillary structure. Many of the cells were distended by supranuclear secretory globules. In the fleshy areas there were small cysts lined by similar epithelium, and many of these showed irregularity in size. Hyperchromatism was a feature and there were mitotic figures in moderate numbers. The stroma was of vascular connective tissue. The appearances were those of a cystadenocarcinoma (Figs. II and III).

FIG. II. Photomicrograph of tumour showing papillary structure. (x 90)

FIG. III. Photomicrograph of tumour showing irregular neoplastic acini. Supranucleolar secretory globules are prominent. (x 140)

DISCUSSION

The vast majority of pancreatic neoplasms are solid carcinomata. Cystic tumours are most often benign, examples of these having been recorded relatively frequently. Such reports are represented by those of Carling and Hicks (1926), Bowers *et alii* (1942), Herrman and Asbell (1949), Miller *et alii* (1951), Mozan (1951), and Burk and Hill (1952).

Malignant cystic tumours are much more uncommon. Lichtenstein (1934) could find no previous case in the American literature, while Miller *et alii* (1951), found only one cystadenocarcinoma among 202 primary tumours of the pancreas at the Mayo Clinic. Kennard (1941) reported a case in detail and reviewed the literature. He found only 21 acceptable recorded cases. This author states an incidence of 9 per cent. of cystic tumours. Mahorner and Mattson (1931) found four cases of malignancy among 88 pancreatic cysts treated surgically; an incidence of 4.5 per cent.

It appears that the sexes are affected equally by the condition. This was found in the review of Kennard (1941), and more recently in that of Mason *et alii* (1954). In the cases of Kennard's series, age varied between 34 and 79 with an average of 53.

Kennard (1941) states that there is often a long history of abdominal discomfort, pain being due to pressure on neighbouring organs. In our case, the length of the history is doubtful, although symptoms may have been present for two years. Mason *et alii* (1954) suggest the possibility that a benign cystadenoma may become malignant after a long period. Lichtenstein (1934) reported a case in which a simple lesion was present for six years, malignant change being found at necropsy. Clinically, the mass in the pancreas had been regarded as an enlarged spleen. It is of interest that the same diagnostic error was made in our case.

Kennard (1941) and Mason (1954) state that the tumours are situated most often in the body and tail of the pancreas, the head being the most unusual site. At operation the mass most often presents between the stomach and transverse colon, as it did in the present case, or through the small omentum.

Mason *et alii* (1954) consider that cysts of the pancreas originate in ectopic embryonic cells as proliferations of ductal or acinar epithelium. Metaplasia of epithelium however appears to be a much more likely explanation. Such epithelial metaplasia occurs in other glandular organs, and the similarity to ovarian tumours appears merely fortuitous.

Although rare, cystic pancreatic tumours appear worthy of consideration in cases where the diagnosis is obscure, and vague upper abdominal symptoms predominate. Because of malignant alteration in the cysts, early diagnosis seems important. It would appear that the prognosis is quite good, widespread metastases being the exception.

SUMMARY

A case of cystadenocarcinoma of the pancreas is presented and previous reports reviewed briefly. The tumour was successfully treated by surgical excision after a preliminary biopsy. At the first laparotomy the nature of the lesion was not recognized.

It is suggested that cystic lesions of the pancreas should be considered in the differential diagnosis of vague upper abdominal discomfort.

ACKNOWLEDGEMENTS

We wish to thank the Superintendent of the Dunedin Hospital for permission to use the clinical records; Dr. R. A. Rodda for helpful criticism; and Mrs. D. Lemon and Mr. G. Brooks for the photographs.

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Books Reviewed

THE LIFE OF HUGH OWEN THOMAS.

By DAVID LE VAY, M.S.(Lond.), F.R.C.S.(Eng.). Edinburgh: E. & S. Livingstone Ltd., 1956. 9" x 6½", vii plus 136 pp., frontispiece and 27 illustrations. Price: 25s. stg.

Modern orthopaedic surgery owes a tremendous debt to Hugh Owen Thomas. No less a debt is owed to Robert Jones, his nephew, who so ably carried on Thomas' principles. During his lifetime Thomas was looked down on, even despised, by his fellow surgeons and certainly did not receive the professional acclaim that he was entitled to and had every right to expect. This was due to many factors of which one of the most important was that Thomas was extremely egocentric and very prone to write blistering attacks on the surgical acumen and professional skill of his fellow surgeons. On the other hand there is no doubt that there was much jealousy caused by his uncanny ability to treat and cure the many difficult cases who came to him when others had failed to produce a satisfactory result. Despised he may have been by his surgical brethren but he was revered by the poor of Liverpool for whom he worked so hard and served so well. His clinics at 11 Nelson Street became famous amongst rich and poor alike, for his practice was enormous and he was visited by many surgeons from overseas interested in his methods.

Thomas was unconventional in dress, manners and in methods of treatment but he obtained results in the most difficult orthopaedic problems, often by relatively simple methods. To have watched Thomas conduct his busy clinics must have been a wonderful experience. While he was alive he received the plaudits of his patients but it was not until after his death that he was given his rightful place as a founder of modern orthopaedic surgery.

Le Vay's life of Thomas is well written and brings out all aspects of his character. Both author and publisher deserve our thanks and congratulations for this admirable biography of a great figure. It should be read and studied by all surgeons.

A MANUAL OF ANAESTHETIC TECHNIQUES.

By WILLIAM J. PRYOR, M.B., Ch.B.(N.Z.), F.F.A.R.C.S.(Eng.), D.A.(Eng.), M.F.A., R.A.C.S., with a Foreword by J. H. T. CHALLIS, M.R.C.S.(Eng.), L.R.C.P.(Lond.), F.F.A.R.C.S.(Eng.), D.A.(Eng.). Bristol: John Wright & Sons Ltd. 1956. 8½" x 5½", 224 pp., 77 illustrations. Price: 27s. 6d. net.

The author, in his preface, states that this book is intended primarily for House Surgeons and Registrars. Accordingly it is written in a dogmatic manner and at times the more experienced reader will not agree with statements that appear in the text. The style is verging on that of a summary and the English, at times, is distinctly "racey." Such phrases as "the patient is too light" frequently appear.

One of the greatest defects is in the references at the end of each chapter. No numbers appear in the text and a reader, wishing to obtain further information on a subject, would be forced to consult several journals. For example, in Chapter IV (Agents used in Anaesthesia) such subjects as Ether, Carbon Dioxide, Pethidine, Gallamine and Methedrine are discussed. Eleven references are given without titles of the articles and with no indication as to which subject is covered by each reference.

Allowing for these defects, this volume, published at a reasonable price, should achieve considerable popularity with recent graduates anxious to acquire some knowledge of anaesthetic technique.

THIOPENTONE AND OTHER THIOBARBITURATES.

By JOHN W. DUNDEE M.D., F.F.A.R.C.S., D.A. Edinburgh and London: E. & S. Livingstone Ltd., 1956. 8½" x 5½", 312 pp., 59 illustrations. Price: 22s. 6d. net.

This book presents a happy combination of research and clinical material, both largely from the author's own experience. In each chapter, the research material which is of practical use to the anaesthetist is set out in bold type. For completeness facts of more academic interest are included, but in smaller type. The research material is followed by clinical applications in each case.

Thiopentone is a drug about which a large literature has accumulated. This book brings it together and presents it to the reader in a form which is most valuable.

The more recently introduced thiobarbiturates are briefly discussed towards the end of the book, as are such drugs as Viadril which are not barbiturates.

Every anaesthetist should study this volume with care as it presents the problems that can arise from the administration of thiopentone and suggests methods of avoiding complications.

TECHNIQUES IN BLOOD GROUPING.

By IVOR DUNSFORD and C. CHRISTOPHER BOWLEY, M.B., B.S., M.R.C.O.G., with Preface by R. R. RACE, F.R.S. Edinburgh and London: Oliver & Boyd, 1955. 9" x 6½", 250 pp., 26 illustrations. Price: 36s. 9d.

The phenomenal extension, in recent years, of knowledge of the blood group factors and increased use of blood transfusion have been associated with even more numerous and complicated technical procedures, descriptions of which are widely dispersed in various journals.

In "Techniques in Blood Grouping," Mr. I. Dunsford, the Senior Scientific Officer, and Dr. C. C. Bowley, Director of the Sheffield Regional Blood Transfusion Centre, and lecturers respectively at the College of Technology and University, have done great service to workers in this field by presenting, in one small book, concise accounts of the basic principles and established facts, followed by systematic detailed descriptions of the techniques used at the Sheffield Centre.

This publication reflects both the academic stature and the vast practical experience of its authors, and the quality of the work done at the Sheffield Centre has resulted in international repute. The breadth of its scope is indicated in Section I of Mr. Dunsford's and Dr. Bowley's book, which includes chapters on the principles of blood grouping, the nature of human red cell antigens, and iso-antibodies, the factors affecting blood grouping reactions, methods

of detecting antigens and antibodies, apparatus, causes of error, controls, provision of anti-sera, the Coombs test, Blood Bank organisation (including record keeping), ante-natal serology, serological diagnosis of haemolytic disease of the new born, and teaching, with suggested plans for evening classes, a short basic course for hospital laboratory workers, and an advanced and comprehensive course in blood transfusion techniques.

Section II describes, step by step, details of 80 techniques set out in numerical order for ease of reference from one to another. They range, to mention but a few, from the elementary but essential technique (No. 1) for proper cleaning of glassware (incidentally, the authors emphasize that a dirty slide can cause a false reaction), preparation, storage and standardization of reagents, including anti-sera for identifying the various blood factors (A B O, Rh, MN and others) to ante-natal serology, compatibility tests including those which pose special problems such as for children under 6 months and in haemolytic anaemia, serological investigation of transfusion reactions, and the identification of rare, or mixed antibodies (No. 80).

Section III is a useful and now-a-days very necessary glossary, arranged alphabetically, of over 500 terms used by blood group workers.

The book is attractively printed in clear type, and has an ingenious form of binding which ensures that it will stay open at any page, if placed on the bench for consultation, so that any technique described in it may be followed as systematically as it is set out. This format is in keeping with the authors' statement that it is intended primarily as a laboratory manual. In spite of this statement, however, there is much in their book that would interest those concerned with general rather than specific laboratory problems of transfusion; a perusal of it would indicate the complexity of the latter, and the responsibility and, often, stress, which devolves on those in charge of the laboratory tests. For instance, the complete identification, in accordance with up-to-date knowledge and technique, of all the blood factors in any individual's red cells, or, in some cases, the elimination of any possible incompatibility between the blood of a prospective recipient and (perhaps several) donors, may be not only an extremely time-consuming procedure, but also, one which requires considerable knowledge, and perhaps ingenuity, adequate laboratory facilities, and ready access to a comprehensive range of blood samples of known blood factor composition to serve as "controls." It is sometimes difficult, in relation to clinical demands or available facilities and trained staff, to avoid a sense of the sheer impracticability of such satisfying complete investigations, ensuring as much serological safety as present-day techniques can give. For these reasons, decisions may have to be made as to whether, under the circumstances of any individual case, the degree of risk involved in time-saving "short cuts" or other departures from the ideal is justified, as being in the best interest of the patient. Some facets of this problem, such as the greater risks of incompatibility of donor blood for "dangerous recipients" (e.g. persons with a history of previous transfusions, and some parous women), and relatively rapid tests, *for emergency use only* (the authors' italics), are dealt with in this book.

There is little, if anything, to criticize, and much more which could be commented on favourably, in this unique and valuable publication. Possibly, in future editions, some spare pages could be inserted for notes which those who keep it open on their benches might wish to insert from time to time.

BODY FLUIDS IN SURGERY.

By W. A. WILKINSON, Ch.M., F.R.C.S.E. Edinburgh: E. & S. Livingstone Ltd., 1955. 8½" x 5½", ix plus 212 pp., 28 tables, 7 figures: Price: 16s. stg.

This book on fluid therapy is written by a practising surgeon. It has been written primarily for those responsible for the care of surgical patients in the belief that the detailed management of disturbances of fluid balance in his patients rightly remains the responsibility of the surgeon.

The object is to provide sufficient information for a basic understanding of body fluids in health and disease and to give an account of the management of disturbances of fluid balance which occur in surgical patients.

In setting down the theoretical basis of the subject, the author has been deft in culling out most of the relevant information from the vast literature of the subject and setting it down in a compact and readable form. The list of references provided is not intended to cover the whole subject in detail but it does provide a very adequate coverage for a book of this type.

Basic theory and observations are freely discussed and throughout are correlated with clinical findings and suggested methods of treatment. At the same time there are many common-sense practical observations often so lacking in books on this subject.

Since the author has done some original work in the subject, it is not to be wondered that he stresses some personal views which are not fully accepted by all working in the field, e.g the superiority of Dextran over normal human serum in the treatment of burns. Not everyone will agree that thirst in the post-operative period is never allayed by 2 litres of 5 per cent. dextrose in the first twenty-four hours.

In discussing management of patients he advocates a very conservative approach to intravenous therapy and one gains the impression that it should only be used when peripheral circulatory failure is imminent or obvious signs of dehydration are present. This is contradictory to his statement that prophylaxis is all important in this field. He gives a particularly conservative approach to intravenous therapy in intestinal obstruction.

It is disappointing that the practising surgeon, who is obviously thoughtful, has not laid stress on the importance of respiratory physiology in relation to the management of severe imbalance and one draws the conclusion that the importance of a dextrous anaesthetist in handling these cases has not been appreciated.

In presenting basic theory and observations the author fulfils his object very well but in discussing management he presents the views of a surgeon who is very conservative in his use of intravenous therapy.

LYMPATHICS, LYMPH AND LYMPHOID TISSUE.

By J. M. YOFFEY and F. C. COURTICE. London: Edward Arnold (Publishers) Ltd., 1956. 9½" x 6", vii plus 510 pp., 99 illustrations. Price: 97s. 3d.

This is the second edition of a monograph by C. K. Drinker and J. M. Yoffey which appeared in 1940. The place of the late Dr. Drinker has been taken by F. C. Courtice.

This edition is somewhat larger than the first and presents in eminently readable form the main features of modern knowledge of the lymphatic system.

The introductory chapter deals with general features of the lymphatic system and following this there are chapters dealing with the formation of lymph, lymph flow, the cell content of lymph and the lymphocyte. There are general sections dealing with significance of lymphatics and lymphoid tissue and a final chapter on practical considerations.

Many problems of fundamental importance, such as the permeability of capillaries and lymphatics, the size and form of various protein molecules and the nature and characteristics of various lipids are considered in detail. Not only are the lymphatic vessels of various organs of the body discussed, but in the verious sections a considerable amount of information on the physiology of these structures is given. Attention is paid to the serous cavities and, indeed, much valuable information regarding the physiology of many tissues will be found.

The book is well produced, the various sections being clearly set out. There is a good bibliography at the end of each chapter. The illustrations in the form of drawings, graphs, photographs and photomicrographs are clearly produced and illustrate well the relevant features.

This volume will be found to be of considerable value, not only to the student, but to the practitioner. Its contents is of particular significance for the surgeon. The problems are dealt with from the point of view of the experienced general physiologist and, from this point of view, apart from the special information available on the lymphatic system itself, is strongly recommended to those who are interested in the basic mechanisms of the tissues with which they deal.

DISEASES OF THE HEART AND CIRCULATION.

By PAUL WOOD, O.B.E., M.D., F.R.C.P. Second Edition. London: Eyre and Spottiswoode Ltd., 1956. 9½" x 6", xxxviii plus 1,005 pp., many illustrations. Price: £5 5s. (stg.).

This is the second and enlarged edition of the book that was first published in 1950. It has been revised and considerably enlarged.

It is an excellent presentation of heart disease and is a standard British work on the subject. It is primarily a book written by a physician for physicians, but with the extraordinary advances in cardiac surgery of the last decade the time has gone when knowledge of cardiac disease can reasonably be regarded as "medical."

The first two chapters deal with symptoms and physical signs. These are clearly presented and are of general interest. The next three deal with electrocardiography, radiography and the large group of special investigations ranging from determination of circulation times and examination by arteriograms up to ballisto-cardiography.

The subsequent chapters deal with such signs or symptoms of heart disease as disorders of cardiac rhythm or heart failure, certain general and secondary cardiac disturbances such as hypertensive heart disease and the various specific conditions such as congenital heart disease, rheumatic disease and the like.

Other parts give an account of diseases of the pericardium and of the great vessels as well as of some pulmonary conditions. There is a section on the heart in disturbances of the thyroid gland and an excellent final chapter on cardiovascular disturbances associated with psychiatric states.

Throughout, the material is excellently presented. Statements are made clearly and precisely and, partly because of this, effectively and forcefully. Where possible, a definite opinion is given and where matters are still in doubt, opposing viewpoints are stated in a pithy manner. The text is a pleasure to read and information can be obtained with a minimum of effort. The literature, particularly of recent years, is well covered and is also dealt with in a succinct manner. Reference to recent work in various parts of the world is thoroughly up to date, as is shown not only in the section on special investigations but also in such sections as that on dissecting aneurysm.

This volume is very well produced with clear text and excellent illustrations. There is a thoroughly adequate index. The work can be unreservedly recommended to all clinicians; even from the point of view of the surgeon it is probably taking too narrow a view to say merely that it should be in the hands of all thoracic surgeons.

SURGERY FOR NURSES.

By JAMES MORONEY, M.B., Ch.B., F.R.C.S.(Eng.), L.R.C.P.(Lond.). Fourth Edition. Edinburgh: E. & S. Livingstone Ltd., 1956. 8½" x 5½", 703 pp., 593 illustrations. Price: 27s. 6d.

In this volume student nurses are fortunate to have available a complete reference work in which the subjects of surgical practice and surgical nursing have been skilfully combined. The material has been presented in a most readable form in large clear type and the profusion of excellent illustrations has ensured that every point has been well made. The author has not attempted to describe the detailed nursing practice of one particular school, but has outlined the guiding principle used by every nursing school. Tutors need not be afraid that nurses will be confused by the minor differences in detail between locally adopted nursing techniques and those described in this volume. A chapter on obstetrics has been included which will answer most of the questions a general nurse will be expected to answer during the course of her work.

Book Received

ALFRED HOSIPTAL CLINICAL REPORTS. Volume 6.

Melbourne, Australia: Alfred Hospital, 1956. 10" x 6", 143 pp., various figures in each section.

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